
```
TCACGTAAAA AGGGTATCTA GAATTATGAT GATTACTCTG CGCAAACTTC CTCTGGCGGT TGCCGTCGCA GCGGGCGTAA TGTCTGCTCA GGCCATGGCC
AGTGCATTTT TCCCATAGAT CTTAATACTA CTAATGAGAC GCGTTTGAAG GAGACCGCCA ACGGCAGCGT CGCCCGCATT ACAGACGAGT CCGGTACCGG
                          MetMe tIleThrLeu ArgLysLeuP roLeuAlaVa lAlaValAla AlaGlyValM etSerAlaGl nAlaMetAla
                          ^Start of lamB signal sequence

GGTCCCGAAA CTCTGTGCGG TGCTGAACTG GTTGACGCTC TGCAGTTCGT ATGTGGTGAT CGAGGCTTCC TGTTCAACAA ACCGACTGGG GCTGGATCCT
CCAGGGCTTT GAGACACGCC ACGACTTGAC CAACTGCGAG ACGTCAAGCA TACACCACTA GCTCCGAAGG ACAAGTTGTT TGGCTGACCC CGACCTAGGA
GlyProGluT hrLeuCysGl yAlaGluLeu ValAspAlaL euGlnPheVa lCysGlyAsp ArgGlyPheL euPheAsnLy sProThrGly AlaGlySerSer
^Start of IGF-I (Y24L,Y31A)

CCTCTCGTCG TGCTCCCCAG ACTGGTATTG TTGACGAATG CTGCTTTCGT TCTTGCGACC TGCGTCGTCT GGAAATGTAT TGCGCTCCCC TGAAACCCGC
GGAGAGCAGC ACGAGGGGTC TGACCATAAC AACTGCTTAC GACGAAAGCA AGAACGCTGG ACGCAGCAGA CCTTTACATA ACGCGAGGGG ACTTTGGGCG
  SerArgAr gAlaProGln ThrGlyIleV alAspGluCy sCysPheArg SerCysAspL euArgArgLe uGluMetTyr CysAlaProL euLysProAla

TAAATCTGCT TAGAAGCTCC TAACGCTCGG TTGCCGCCGG GCGTTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT AATGCGGTAG
ATTTAGACGA ATCTTCGAGG ATTGCGAGCC AACGGCGGCC CGCAAAAAAT AACAATTGAG TACAAACTGT CGAATAGTAG CTATTCGAAA TTACGCCATC
 LysSerAla Am*
```

Nucleotide and Amino Acid Sequence of the LamB Signal Sequence and IGF-I (Y24L,Y31A)

FIG. 1

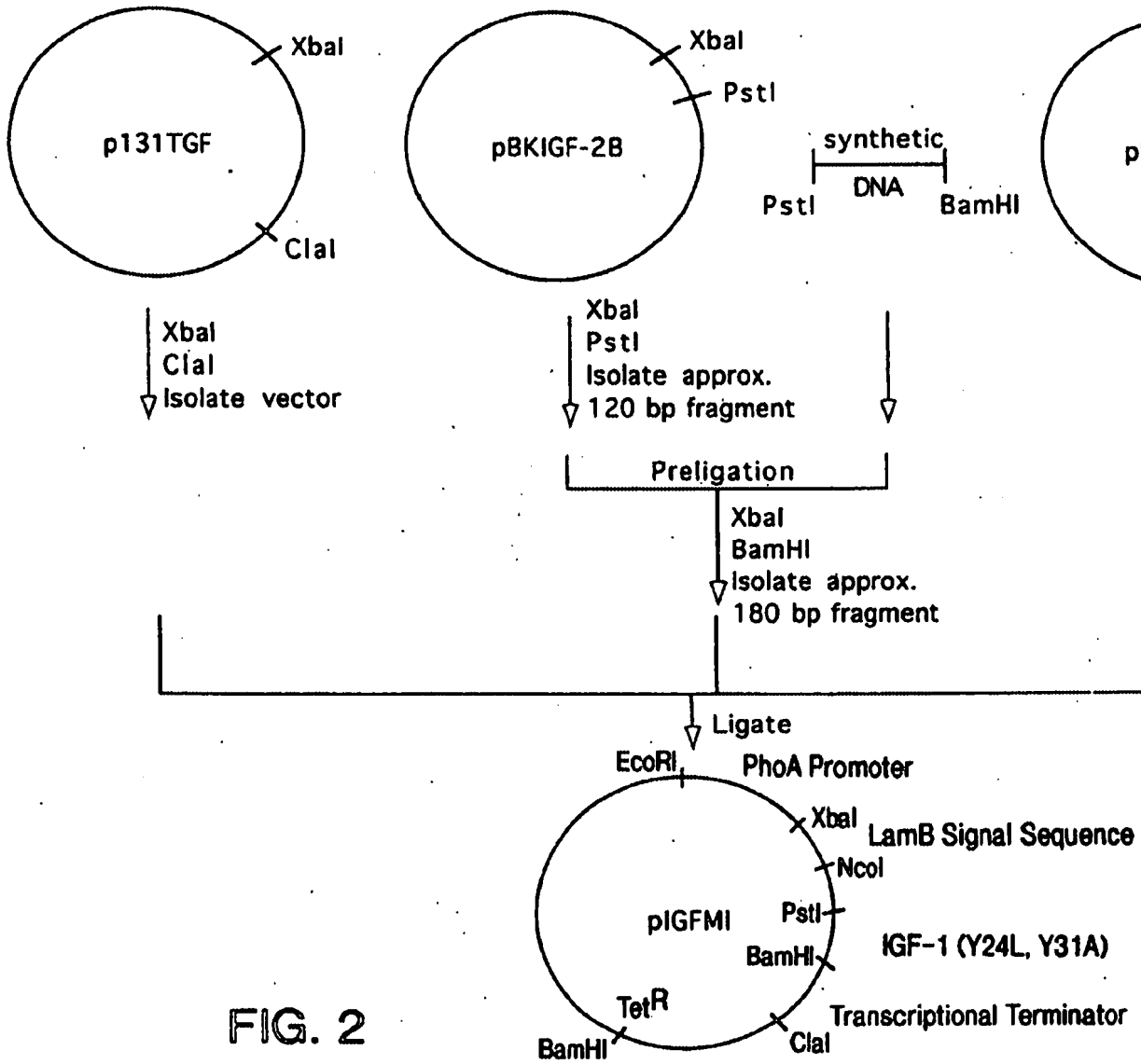

FIG. 2

plasmid IGFMI
length: 5115 (circular)

```
   1 GAATTCAACT TCTCCATACT TTGGATAAGG AAATACAGAC ATGAAAAATC TCATTGCTGA GTTGTTATTT AAGCTTGCCC AAAAAGAAGA AGAGTCGAAT
     CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCTG TACTTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTTCTTCT TCTCAGCTTA

 101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
     CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTTAC TGGTTGTCGC CAACTAACTA GTCCATCTCC

 201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA
     CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

 301 AAAAGTTAAT CTTTTCAACA GCTGTCATAA AGTTGTCACG GCCGAGACTT ATAGTCGCTT TGTTTTTATT TTTTAATGTA TTTGTAACTA GTACGCAAGT
     TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

 401 TCACGTAAAA AGGGTATCTA GAATTATGAT GATTACTCTG CGCAAACTTC CTCTGGCGGT TGCCGTCGCA GCGGGCGTAA TGTCTGCTCA GGCCATGGCC
     AGTGCATTTT TCCCATAGAT CTTAATACTA CTAATGAGAC GCGTTTGAAG GAGACCGCCA ACGGCAGCGT CGCCCGCATT ACAGACGAGT CCGGTACCGG
   1                          MetMe tIleThrLeu ArgLysLeuP roLeuAlaVa lAlaValAla AlaGlyValM etSerAlaGl nAlaMetAla

 501 GGTCCCGAAA CTCTGTGCGG TGCTGAACTG GTTGACGCTC TGCAGTTCGT ATGTGGTGAT CGAGGCTTCC TGTTCAACAA ACCGACTGGG GCTGGATCCT
     CCAGGGCTTT GAGACACGCC ACGACTTGAC CAACTGCGAG ACGTCAAGCA TACACCACTA GCTCCGAAGG ACAAGTTGTT TGGCTGACCC CGACCTAGGA
  26 GlyProGluT hrLeuCysGl yAlaGluLeu ValAspAlaL euGlnPheVa lCysGlyAsp ArgGlyPheL euPheAsnLy sProThrGly AlaGlySerSer

 601 CCTCTCGTCG TGCTCCCCAG ACTGGTATTG TTGACGAATG CTGCTTTCGT TCTTGCGACC TGCGTCGTCT GGAAATGTAT TGCGCTCCCC TGAAACCCGC
     GGAGAGCAGC ACGAGGGGTC TGACCATAAC AACTGCTTAC GACGAAAGCA AGAACGCTGG ACGCAGCAGA CCTTTACATA ACGCGAGGGG ACTTTGGGCG
  60   SerArgAr gAlaProGln ThrGlyIleV alAspGluCy sCysPheArg SerCysAspL euArgArgLe uGluMetTyr CysAlaProL euLysProAla

 701 TAAATCTGCT TAGAAGCTCC TAACGCTCGG TTGCCGCCGG GCGTTTTTTA TTGTTAACTC ATGTTTGACA GCTTATCATC GATAAGCTTT AATGCGGTAG
     ATTTAGACGA ATCTTCGAGG ATTGCGAGCC AACGGCGGCC CGCAAAAAAT AACAATTGAG TACAAACTGT CGAATAGTAG CTATTCGAAA TTACGCCATC
  93  LysSerAla Am*

 801 TTTATCACAG TTAAATTGCT AACGCAGTCA GGCACCGTGT ATGAAATCTA ACAATGCGCT CATCGTCATC CTCGGCACCG TCACCCTGGA TGCTGTAGGC
     AAATAGTGTC AATTTAACGA TTGCGTCAGT CCGTGGCACA TACTTTAGAT TGTTACGCGA GTAGCAGTAG GAGCCGTGGC AGTGGGACCT ACGACATCCG

 901 ATAGGCTTGG TTATGCCGGT ACTGCCGGGC CTCTTGCGGG ATATCGTCCA TTCCGACAGC ATCGCCAGTC ACTATGGCGT GCTGCTAGCG CTATATGCGT
     TATCCGAACC AATACGGCCA TGACGGCCCG GAGAACGCCC TATAGCAGGT AAGGCTGTCG TAGCGGTCAG TGATACCGCA CGACGATCGC GATATACGCA

1001 TGATGCAATT TCTATGCGCA CCCGTTCTCG GAGCACTGTC CGACCGCTTT GGCCGCCGCC CAGTCCTGCT CGCTTCGCTA CTTGGAGCCA CTATCGACTA
     ACTACGTTAA AGATACGCGT GGGCAAGAGC CTCGTGACAG GCTGGCGAAA CCGGCGGCGG GTCAGGACGA GCGAAGCGAT GAACCTCGGT GATAGCTGAT
```

FIG. 3A

```
1101 CGCGATCATG GCGACCACAC CCGTCCTGTG GATCCTCTAC GCCGGACGCA TCGTGGCCGG CATCACCGGC GCCACAGGTG CGGTTGCTGG CGCCTATATC
     GCGCTAGTAC CGCTGGTGTG GGCAGGACAC CTAGGAGATG CGGCCTGCGT AGCACCGGCC GTAGTGGCCG CGGTGTCCAC GCCAACGACC GCGGATATAG

1201 GCCGACATCA CCGATGGGGA AGATCGGGCT CGCCACTTCG GGCTCATGAG CGCTTGTTTC GGCGTGGGTA TGGTGGCAGG CCCCGTGGCC GGGGGACTGT
     CGGCTGTAGT GGCTACCCCT TCTAGCCCGA GCGGTGAAGC CCGAGTACTC GCGAACAAAG CCGCACCCAT ACCACCGTCC GGGGCACCGG CCCCCTGACA

1301 TGGGCGCCAT CTCCTTGCAT GCACCATTCC TTGCGGCGGC GGTGCTCAAC GGCCTCAACC TACTACTGGG CTGCTTCCTA ATGCAGGAGT CGCATAAGGG
     ACCCGCGGTA GAGGAACGTA CGTGGTAAGG AACGCCGCCG CCACGAGTTG CCGGAGTTGG ATGATGACCC GACGAAGGAT TACGTCCTCA GCGTATTCCC

1401 AGAGCGTCGA CCGATGCCCT TGAGAGCCTT CAACCCAGTC AGCTCCTTCC GGTGGGCGCG GGGCATGACT ATCGTCGCCG CACTTATGAC TGTCTTCTTT
     TCTCGCAGCT GGCTACGGGA ACTCTCGGAA GTTGGGTCAG TCGAGGAAGG CCACCCGCGC CCCGTACTGA TAGCAGCGGC GTGAATACTG ACAGAAGAAA

1501 ATCATGCAAC TCGTAGGACA GGTGCCGGCA GCGCTCTGGG TCATTTTCGG CGAGGACCGC TTTCGCTGGA GCGCGACGAT GATCGGCCTG TCGCTTGCGG
     TAGTACGTTG AGCATCCTGT CCACGGCCGT CGCGAGACCC AGTAAAAGCC GCTCCTGGCG AAAGCGACCT CGCGCTGCTA CTAGCCGGAC AGCGAACGCC

1601 TATTCGGAAT CTTGCACGCC CTCGCTCAAG CCTTCGTCAC TGGTCCCGCC ACCAAACGTT TCGGCGAGAA GCAGGCCATT ATCGCCGGCA TGGCGGCCGA
     ATAAGCCTTA GAACGTGCGG GAGCGAGTTC GGAAGCAGTG ACCAGGGCGG TGGTTTGCAA AGCCGCTCTT CGTCCGGTAA TAGCGGCCGT ACCGCCGGCT

1701 CGCGCTGGGC TACGTCTTGC TGGCGTTCGC GACGCGAGGC TGGATGGCCT TCCCCATTAT GATTCTTCTC GCTTCCGGCG GCATCGGGAT GCCCGCGTTG
     GCGCGACCCG ATGCAGAACG ACCGCAAGCG CTGCGCTCCG ACCTACCGGA AGGGGTAATA CTAAGAAGAG CGAAGGCCGC CGTAGCCCTA CGGGCGCAAC

1801 CAGGCCATGC TGTCCAGGCA GGTAGATGAC GACCATCAGG GACAGCTTCA AGGATCGCTC GCGGCTCTTA CCAGCCTAAC TTCGATCACT GGACCGCTGA
     GTCCGGTACG ACAGGTCCGT CCATCTACTG CTGGTAGTCC CTGTCGAAGT TCCTAGCGAG CGCCGAGAAT GGTCGGATTG AAGCTAGTGA CCTGGCGACT

1901 TCGTCACGGC GATTTATGCC GCCTCGGCGA GCACATGGAA CGGGTTGGCA TGGATTGTAG GCGCCGCCCT ATACCTTGTC TGCCTCCCCG CGTTGCGTCG
     AGCAGTGCCG CTAAATACGG CGGAGCCGCT CGTGTACCTT GCCCAACCGT ACCTAACATC CGCGGCGGGA TATGGAACAG ACGGAGGGGC GCAACGCAGC

2001 CGGTGCATGG AGCCGGGCCA CCTCGACCTG AATGGAAGCC GGCGGCACCT CGCTAACGGA TTCACCACTC CAAGAATTGG AGCCAATCAA TTCTTGCGGA
     GCCACGTACC TCGGCCCGGT GGAGCTGGAC TTACCTTCGG CCGCCGTGGA GCGATTGCCT AAGTGGTGAG GTTCTTAACC TCGGTTAGTT AAGAACGCCT

2101 GAACTGTGAA TGCGCAAACC AACCCTTGGC AGAACATATC CATCGCGTCC GCCATCTCCA GCAGCCGCAC GCGGCGCATC TCGGGCAGCG TTGGGTCCTG
     CTTGACACTT ACGCGTTTGG TTGGGAACCG TCTTGTATAG GTAGCGCAGG CGGTAGAGGT CGTCGGCGTG CGCCGCGTAG AGCCCGTCGC AACCCAGGAC

2201 GCCACGGGTG CGCATGATCG TGCTCCTGTC GTTGAGGACC CGGCTAGGCT GGCGGGGTTG CCTTACTGGT TAGCAGAATG AATCACCGAT ACGCGAGCGA
     CGGTGCCCAC GCGTACTAGC ACGAGGACAG CAACTCCTGG GCCGATCCGA CCGCCCCAAC GGAATGACCA ATCGTCTTAC TTAGTGGCTA TGCGCTCGCT

2301 ACGTGAAGCG ACTGCTGCTG CAAAACGTCT GCGACCTGAG CAACAACATG AATGGTCTTC GGTTTCCGTG TTTCGTAAAG TCTGGAAACG CGGAAGTCAG
     TGCACTTCGC TGACGACGAC GTTTTGCAGA CGCTGGACTC GTTGTTGTAC TTACCAGAAG CCAAAGGCAC AAAGCATTTC AGACCTTTGC GCCTTCAGTC

2401 CGCCCTGCAC CATTATGTTC CGGATCTGCA TCGCAGGATG CTGCTGGCTA CCCTGTGGAA CACCTACATC TGTATTAACG AAGCGCTGGC ATTGACCCTG
     GCGGGACGTG GTAATACAAG GCCTAGACGT AGCGTCCTAC GACGACCGAT GGGACACCTT GTGGATGTAG ACATAATTGC TTCGCGACCG TAACTGGGAC
```

FIG. 3B

```
2501 AGTGATTTTT CTCTGGTCCC GCCGCATCCA TACCGCCAGT TGTTTACCCT CACAACGTTC CAGTAACCGG GCATGTTCAT CATCAGTAAC CCGTATCGTG
     TCACTAAAAA GAGACCAGGG CGGCGTAGGT ATGGCGGTCA ACAAATGGGA GTGTTGCAAG GTCATTGGCC CGTACAAGTA GTAGTCATTG GGCATAGCAC

2601 AGCATCCTCT CTCGTTTCAT CGGTATCATT ACCCCCATGA ACAGAAATTC CCCCTTACAC GGAGGCATCA AGTGACCAAA CAGGAAAAAA CCGCCCTTAA
     TCGTAGGAGA GAGCAAAGTA GCCATAGTAA TGGGGGTACT TGTCTTTAAG GGGGAATGTG CCTCCGTAGT TCACTGGTTT GTCCTTTTTT GGCGGGAATT

2701 CATGGCCCGC TTTATCAGAA GCCAGACATT AACGCTTCTG GAGAAACTCA ACGAGCTGGA CGCGGATGAA CAGGCAGACA TCTGTGAATC GCTTCACGAC
     GTACCGGGCG AAATAGTCTT CGGTCTGTAA TTGCGAAGAC CTCTTTGAGT TGCTCGACCT GCGCCTACTT GTCCGTCTGT AGACACTTAG CGAAGTGCTG

2801 CACGCTGATG AGCTTTACCG CAGCTGCCTC GCGCGTTTCG GTGATGACGG TGAAAACCTC TGACACATGC AGCTCCCGGA GACGGTCACA GCTTGTCTGT
     GTGCGACTAC TCGAAATGGC GTCGACGGAG CGCGCAAAGC CACTACTGCC ACTTTTGGAG ACTGTGTACG TCGAGGGCCT CTGCCAGTGT CGAACAGACA

2901 AAGCGGATGC CGGGAGCAGA CAAGCCCGTC AGGGCGCGTC AGCGGGTGTT GGCGGGTGTC GGGGCGCAGC CATGACCCAG TCACGTAGCG ATAGCGGAGT
     TTCGCCTACG GCCCTCGTCT GTTCGGGCAG TCCCGCGCAG TCGCCCACAA CCGCCCACAG CCCCGCGTCG GTACTGGGTC AGTGCATCGC TATCGCCTCA

3001 GTATACTGGC TTAACTATGC GGCATCAGAG CAGATTGTAC TGAGAGTGCA CCATATGCGG TGTGAAATAC CGCACAGATG CGTAAGGAGA AAATACCGCA
     CATATGACCG AATTGATACG CCGTAGTCTC GTCTAACATG ACTCTCACGT GGTATACGCC ACACTTTATG GCGTGTCTAC GCATTCCTCT TTTATGGCGT

3101 TCAGGCGCTC TTCCGCTTCC TCGCTCACTG ACTCGCTGCG CTCGGTCGTT CGGCTGCGGC GAGCGGTATC AGCTCACTCA AAGGCGGTAA TACGGTTATC
     AGTCCGCGAG AAGGCGAAGG AGCGAGTGAC TGAGCGACGC GAGCCAGCAA GCCGACGCCG CTCGCCATAG TCGAGTGAGT TTCCGCCATT ATGCCAATAG

3201 CACAGAATCA GGGGATAACG CAGGAAAGAA CATGTGAGCA AAAGGCCAGC AAAAGGCCAG GAACCGTAAA AAGGCCGCGT TGCTGGCGTT TTTCCATAGG
     GTGTCTTAGT CCCCTATTGC GTCCTTTCTT GTACACTCGT TTTCCGGTCG TTTTCCGGTC CTTGGCATTT TTCCGGCGCA ACGACCGCAA AAAGGTATCC

3301 CTCCGCCCCC CTGACGAGCA TCACAAAAAT CGACGCTCAA GTCAGAGGTG GCGAAACCCG ACAGGACTAT AAAGATACCA GGCGTTTCCC CCTGGAAGCT
     GAGGCGGGGG GACTGCTCGT AGTGTTTTTA GCTGCGAGTT CAGTCTCCAC CGCTTTGGGC TGTCCTGATA TTTCTATGGT CCGCAAAGGG GGACCTTCGA

3401 CCCTCGTGCG CTCTCCTGTT CCGACCCTGC CGCTTACCGG ATACCTGTCC GCCTTTCTCC CTTCGGGAAG CGTGGCGCTT TCTCATAGCT CACGCTGTAG
     GGGAGCACGC GAGAGGACAA GGCTGGGACG GCGAATGGCC TATGGACAGG CGGAAAGAGG GAAGCCCTTC GCACCGCGAA AGAGTATCGA GTGCGACATC

3501 GTATCTCAGT TCGGTGTAGG TCGTTCGCTC CAAGCTGGGC TGTGTGCACG AACCCCCCGT TCAGCCCGAC CGCTGCGCCT TATCCGGTAA CTATCGTCTT
     CATAGAGTCA AGCCACATCC AGCAAGCGAG GTTCGACCCG ACACACGTGC TTGGGGGGCA AGTCGGGCTG GCGACGCGGA ATAGGCCATT GATAGCAGAA

3601 GAGTCCAACC CGGTAAGACA CGACTTATCG CCACTGGCAG CAGCCACTGG TAACAGGATT AGCAGAGCGA GGTATGTAGG CGGTGCTACA GAGTTCTTGA
     CTCAGGTTGG GCCATTCTGT GCTGAATAGC GGTGACCGTC GTCGGTGACC ATTGTCCTAA TCGTCTCGCT CCATACATCC GCCACGATGT CTCAAGAACT

3701 AGTGGTGGCC TAACTACGGC TACACTAGAA GGACAGTATT TGGTATCTGC GCTCTGCTGA AGCCAGTTAC CTTCGGAAAA AGAGTTGGTA GCTCTTGATC
     TCACCACCGG ATTGATGCCG ATGTGATCTT CCTGTCATAA ACCATAGACG CGAGACGACT TCGGTCAATG GAAGCCTTTT TCTCAACCAT CGAGAACTAG
```

FIG. 3C

```
3801 CGGCAAACAA ACCACCGCTG GTAGCGGTGG TTTTTTTGTT TGCAAGCAGC AGATTACGCG CAGAAAAAAA GGATCTCAAG AAGATCCTTT GATCTTTTCT
     GCCGTTTGTT TGGTGGCGAC CATCGCCACC AAAAAAACAA ACGTTCGTCG TCTAATGCGC GTCTTTTTTT CCTAGAGTTC TTCTAGGAAA CTAGAAAAGA

3901 ACGGGGTCTG ACGCTCAGTG GAACGAAAAC TCACGTTAAG GGATTTTGGT CATGAGATTA TCAAAAAGGA TCTTCACCTA GATCCTTTTA AATTAAAAAT
     TGCCCCAGAC TGCGAGTCAC CTTGCTTTTG AGTGCAATTC CCTAAAACCA GTACTCTAAT AGTTTTTCCT AGAAGTGGAT CTAGGAAAAT TTAATTTTTA

4001 GAAGTTTTAA ATCAATCTAA AGTATATATG AGTAAACTTG GTCTGACAGT TACCAATGCT TAATCAGTGA GGCACCTATC TCAGCGATCT GTCTATTTCG
     CTTCAAAATT TAGTTAGATT TCATATATAC TCATTTGAAC CAGACTGTCA ATGGTTACGA ATTAGTCACT CCGTGGATAG AGTCGCTAGA CAGATAAAGC

4101 TTCATCCATA GTTGCCTGAC TCCCCGTCGT GTAGATAACT ACGATACGGG AGGGCTTACC ATCTGGCCCC AGTGCTGCAA TGATACCGCG AGACCCACGC
     AAGTAGGTAT CAACGGACTG AGGGGCAGCA CATCTATTGA TGCTATGCCC TCCCGAATGG TAGACCGGGG TCACGACGTT ACTATGGCGC TCTGGGTGCG

4201 TCACCGGCTC CAGATTTATC AGCAATAAAC CAGCCAGCCG GAAGGGCCGA GCGCAGAAGT GGTCCTGCAA CTTTATCCGC CTCCATCCAG TCTATTAATT
     AGTGGCCGAG GTCTAAATAG TCGTTATTTG GTCGGTCGGC CTTCCCGGCT CGCGTCTTCA CCAGGACGTT GAAATAGGCG GAGGTAGGTC AGATAATTAA

4301 GTTGCCGGGA AGCTAGAGTA AGTAGTTCGC CAGTTAATAG TTTGCGCAAC GTTGTTGCCA TTGCTGCAGG CATCGTGGTG TCACGCTCGT CGTTTGGTAT
     CAACGGCCCT TCGATCTCAT TCATCAAGCG GTCAATTATC AAACGCGTTG CAACAACGGT AACGACGTCC GTAGCACCAC AGTGCGAGCA GCAAACCATA

4401 GGCTTCATTC AGCTCCGGTT CCCAACGATC AAGGCGAGTT ACATGATCCC CCATGTTGTG CAAAAAAGCG GTTAGCTCCT TCGGTCCTCC GATCGTTGTC
     CCGAAGTAAG TCGAGGCCAA GGGTTGCTAG TTCCGCTCAA TGTACTAGGG GGTACAACAC GTTTTTTCGC CAATCGAGGA AGCCAGGAGG CTAGCAACAG

4501 AGAAGTAAGT TGGCCGCAGT GTTATCACTC ATGGTTATGG CAGCACTGCA TAATTCTCTT ACTGTCATGC CATCCGTAAG ATGCTTTTCT GTGACTGGTG
     TCTTCATTCA ACCGGCGTCA CAATAGTGAG TACCAATACC GTCGTGACGT ATTAAGAGAA TGACAGTACG GTAGGCATTC TACGAAAAGA CACTGACCAC

4601 AGTACTCAAC CAAGTCATTC TGAGAATAGT GTATGCGGCG ACCGAGTTGC TCTTGCCCGG CGTCAACACG GGATAATACC GCGCCACATA GCAGAACTTT
     TCATGAGTTG GTTCAGTAAG ACTCTTATCA CATACGCCGC TGGCTCAACG AGAACGGGCC GCAGTTGTGC CCTATTATGG CGCGGTGTAT CGTCTTGAAA

4701 AAAAGTGCTC ATCATTGGAA AACGTTCTTC GGGGCGAAAA CTCTCAAGGA TCTTACCGCT GTTGAGATCC AGTTCGATGT AACCCACTCG TGCACCCAAC
     TTTTCACGAG TAGTAACCTT TTGCAAGAAG CCCCGCTTTT GAGAGTTCCT AGAATGGCGA CAACTCTAGG TCAAGCTACA TTGGGTGAGC ACGTGGGTTG

4801 TGATCTTCAG CATCTTTTAC TTTCACCAGC GTTTCTGGGT GAGCAAAAAC AGGAAGGCAA AATGCCGCAA AAAAGGGAAT AAGGGCGACA CGGAAATGTT
     ACTAGAAGTC GTAGAAAATG AAAGTGGTCG CAAAGACCCA CTCGTTTTTG TCCTTCCGTT TTACGGCGTT TTTTCCCTTA TTCCCGCTGT GCCTTTACAA

4901 GAATACTCAT ACTCTTCCTT TTTCAATATT ATTGAAGCAT TTATCAGGGT TATTGTCTCA TGAGCGGATA CATATTTGAA TGTATTTAGA AAAATAAACA
     CTTATGAGTA TGAGAAGGAA AAAGTTATAA TAACTTCGTA AATAGTCCCA ATAACAGAGT ACTCGCCTAT GTATAAACTT ACATAAATCT TTTTATTTGT

5001 AATAGGGGTT CCGCGCACAT TTCCCCGAAA AGTGCCACCT GACGTCTAAG AAACCATTAT TATCATGACA TTAACCTATA AAAATAGGCG TATCACGAGG
     TTATCCCCAA GGCGCGTGTA AAGGGGCTTT TCACGGTGGA CTGCAGATTC TTTGGTAATA ATAGTACTGT AATTGGATAT TTTTATCCGC ATAGTGCTCC

5101 CCCTTTCGTC TTCAA
     GGGAAAGCAG AAGTT
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FIG. 3D

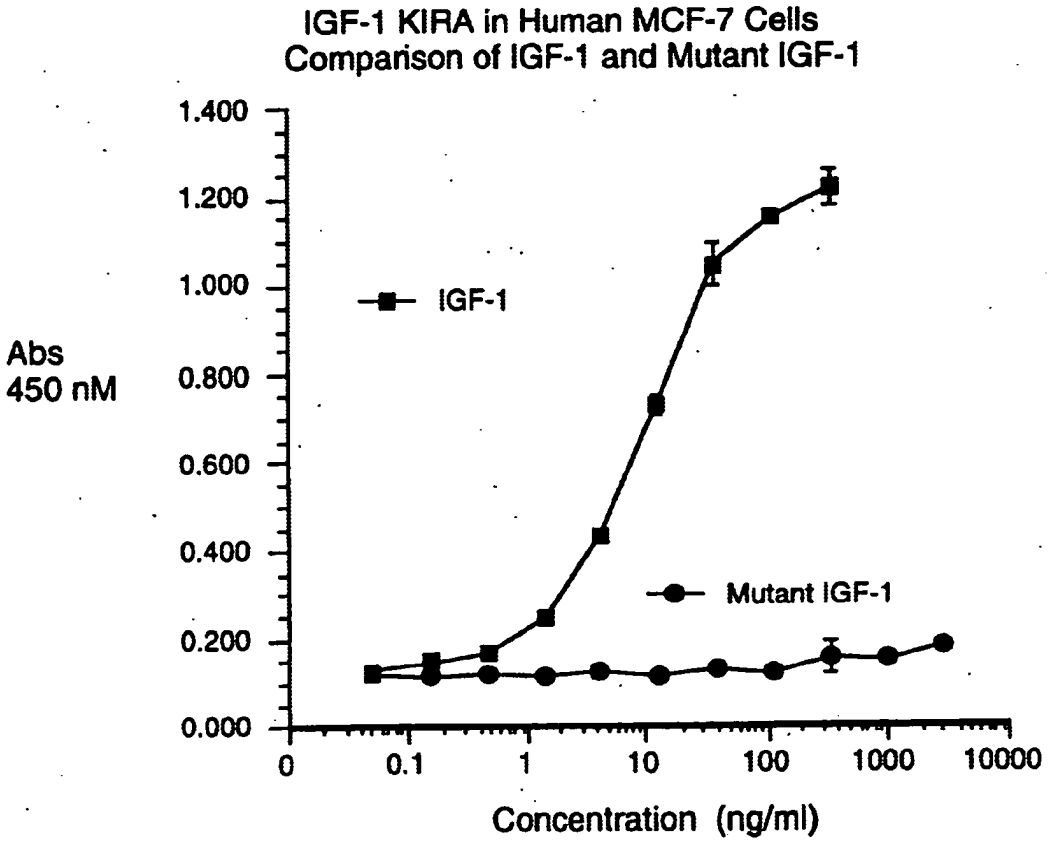


FIG. 4

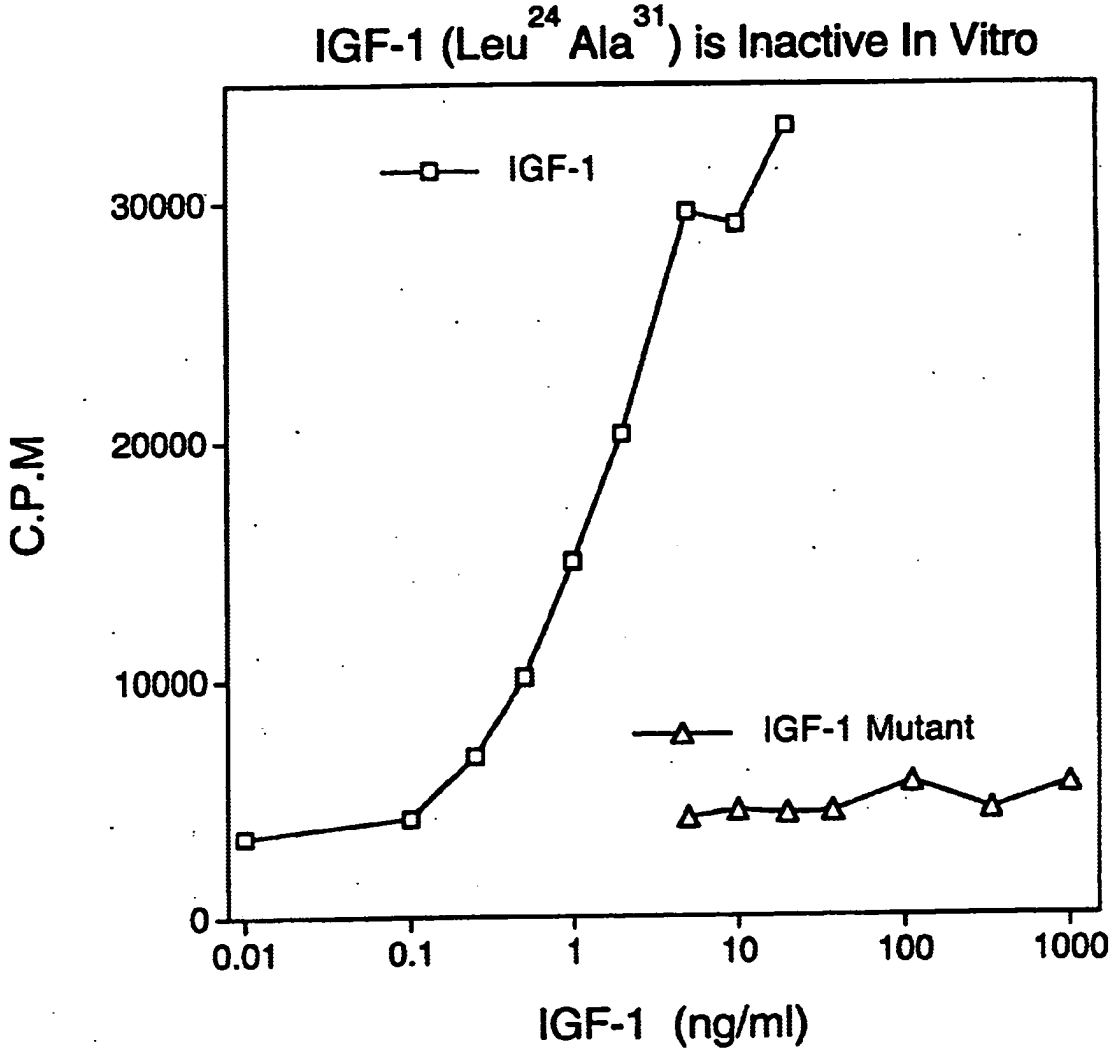


FIG. 5

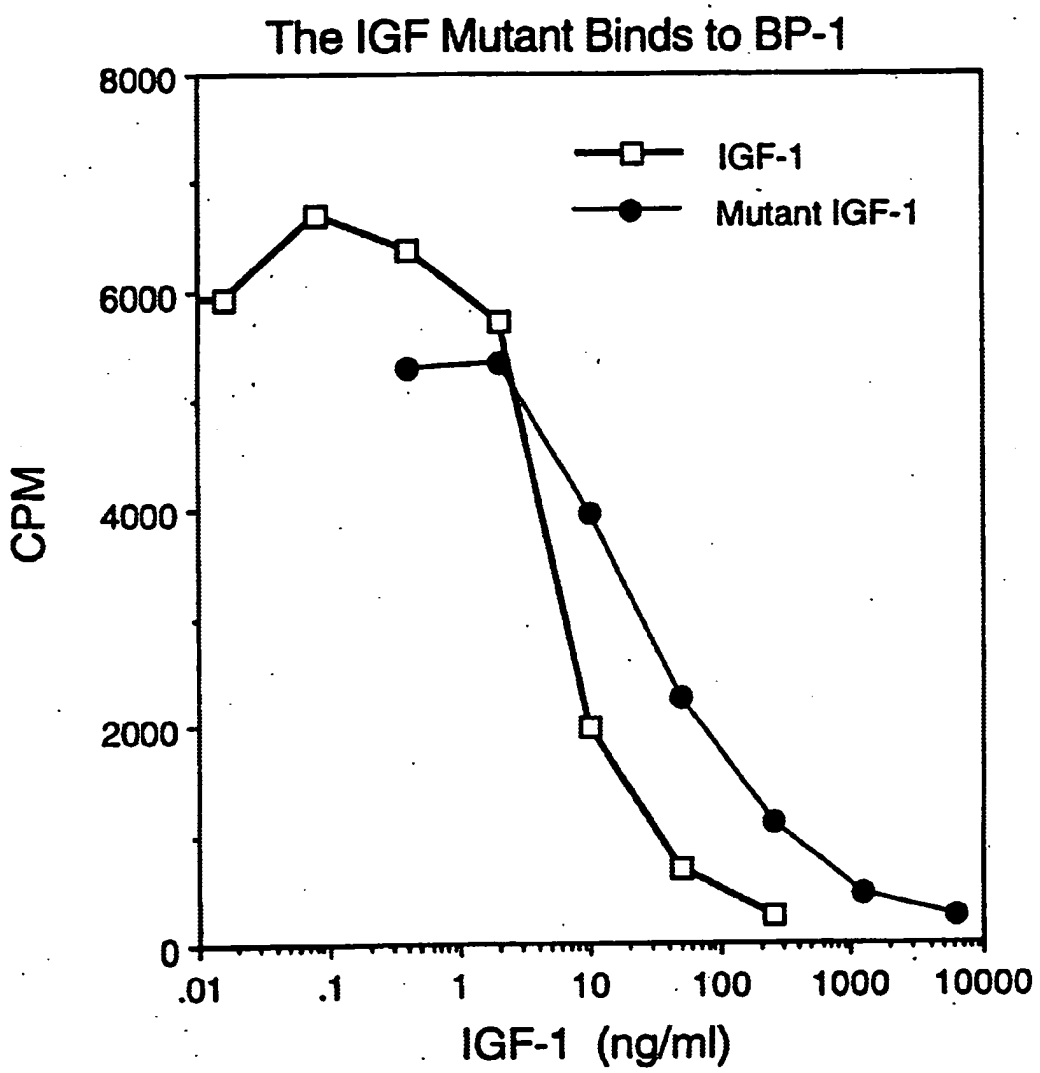


FIG. 6

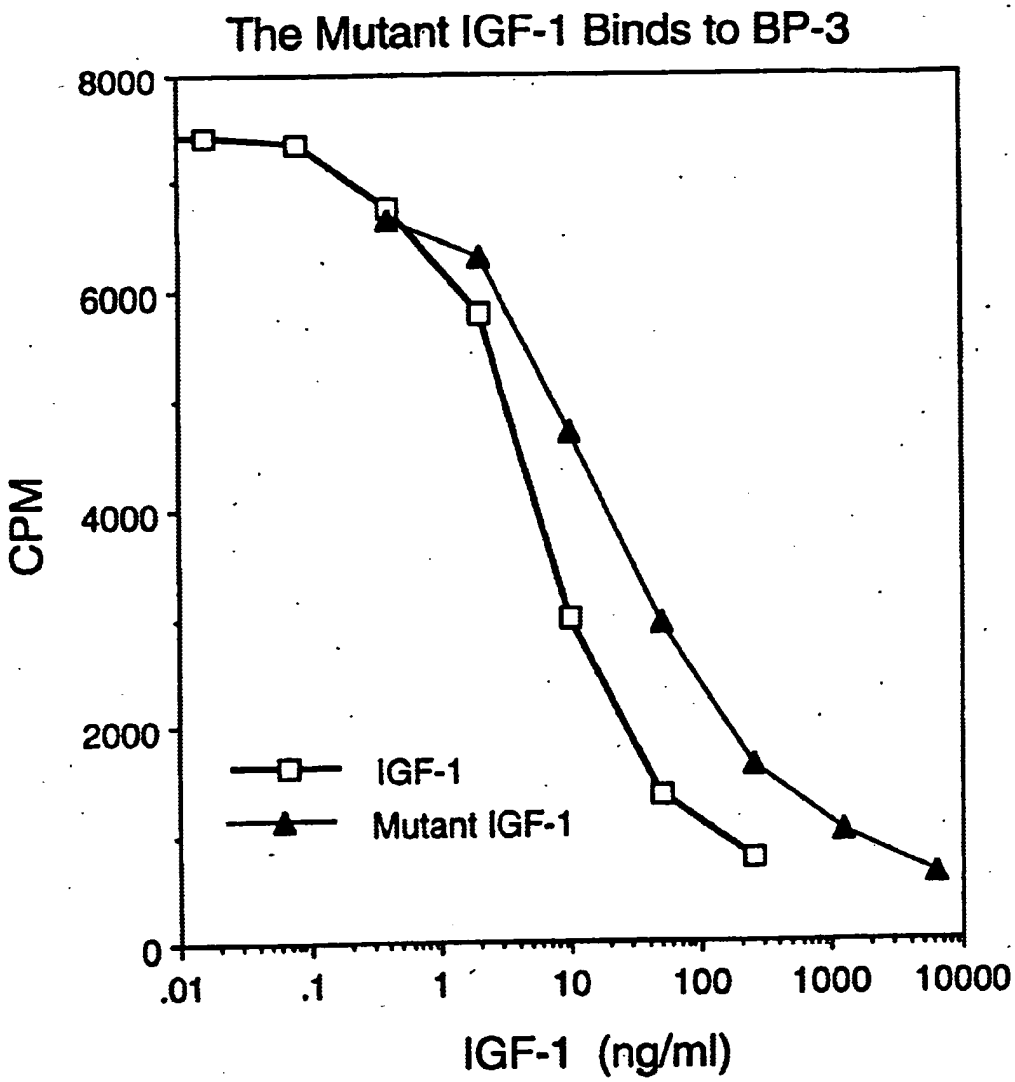


FIG. 7

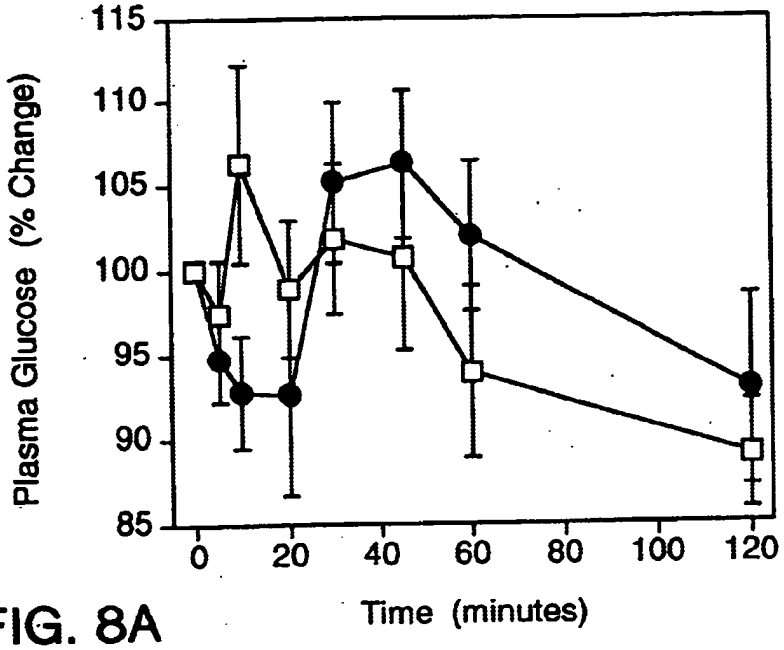


FIG. 8A

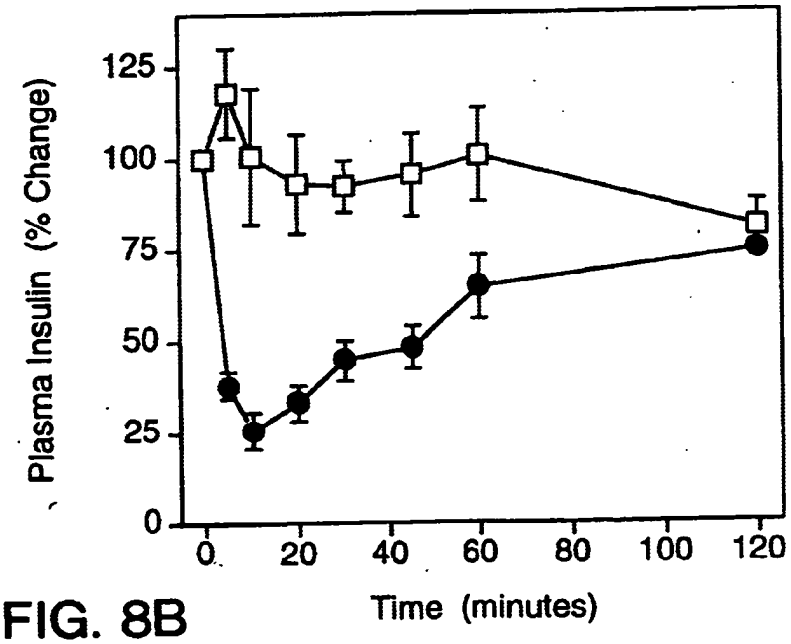


FIG. 8B

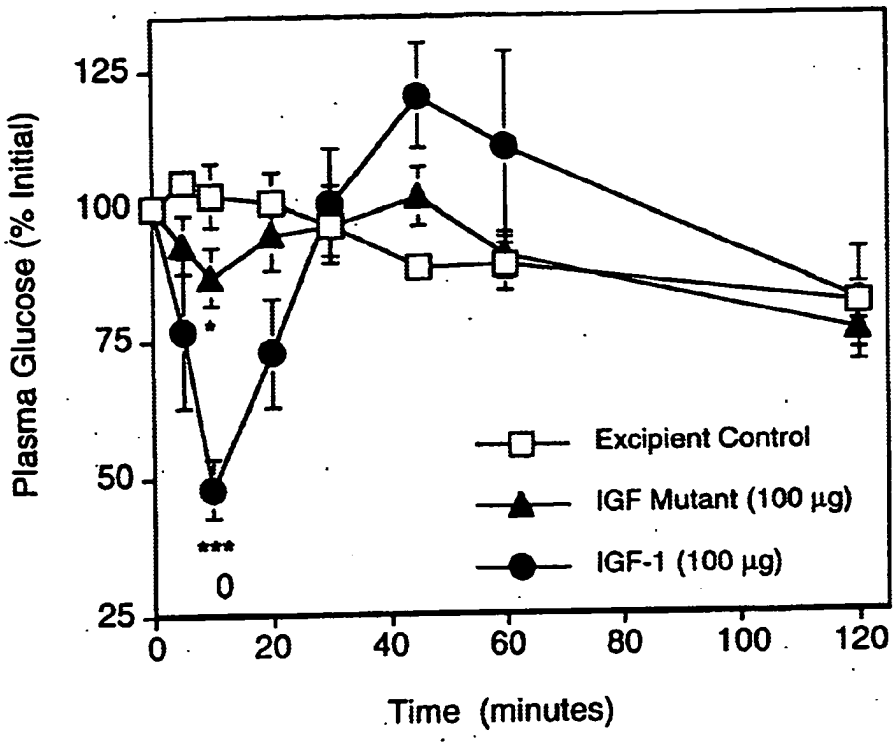


FIG. 9A

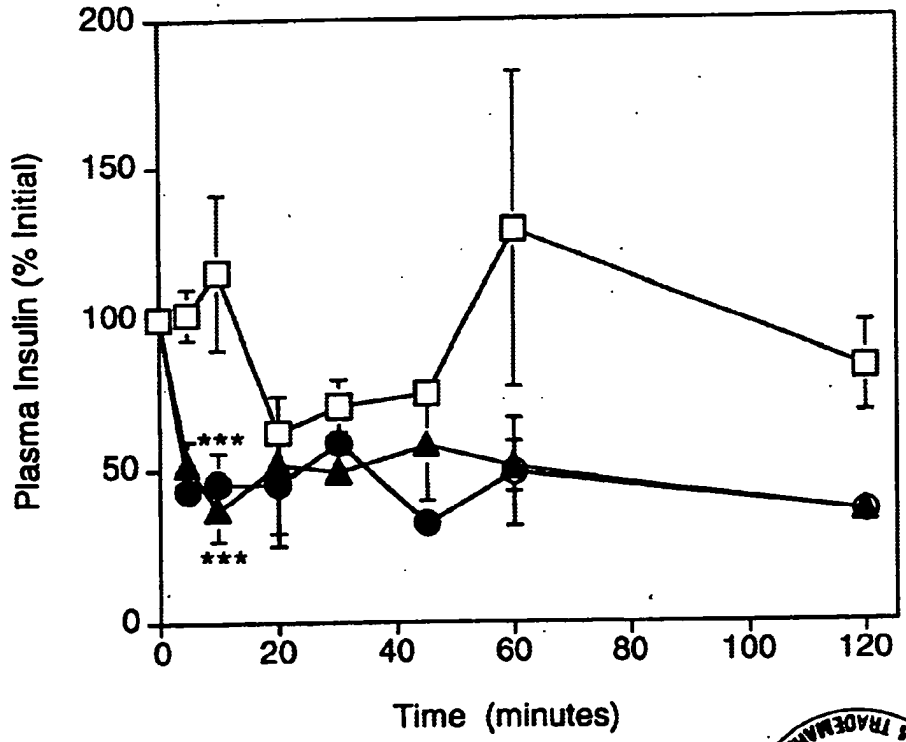


FIG. 9B

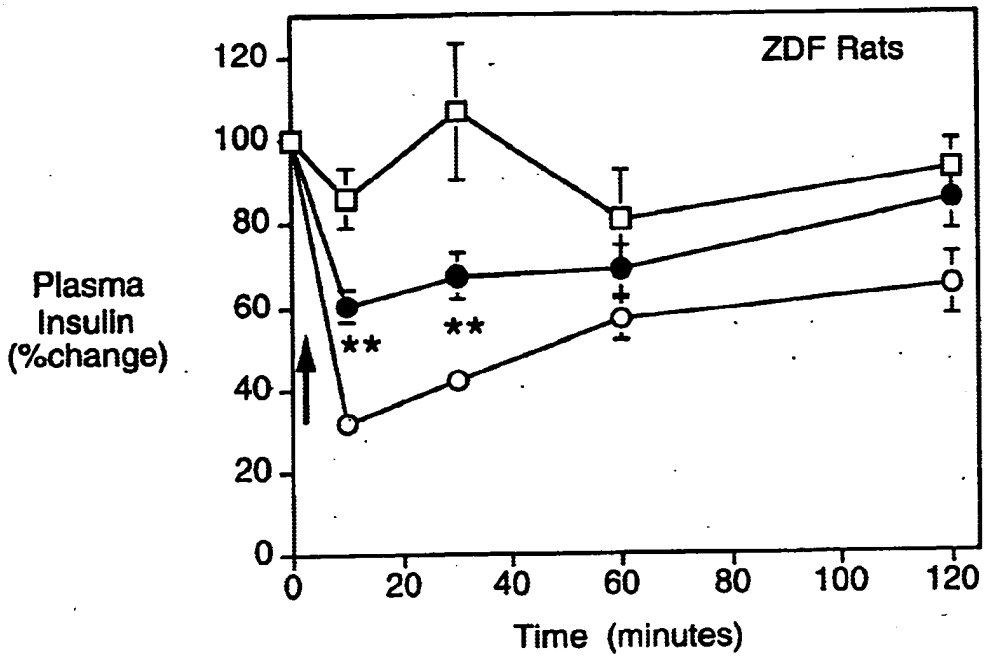


FIG. 10A

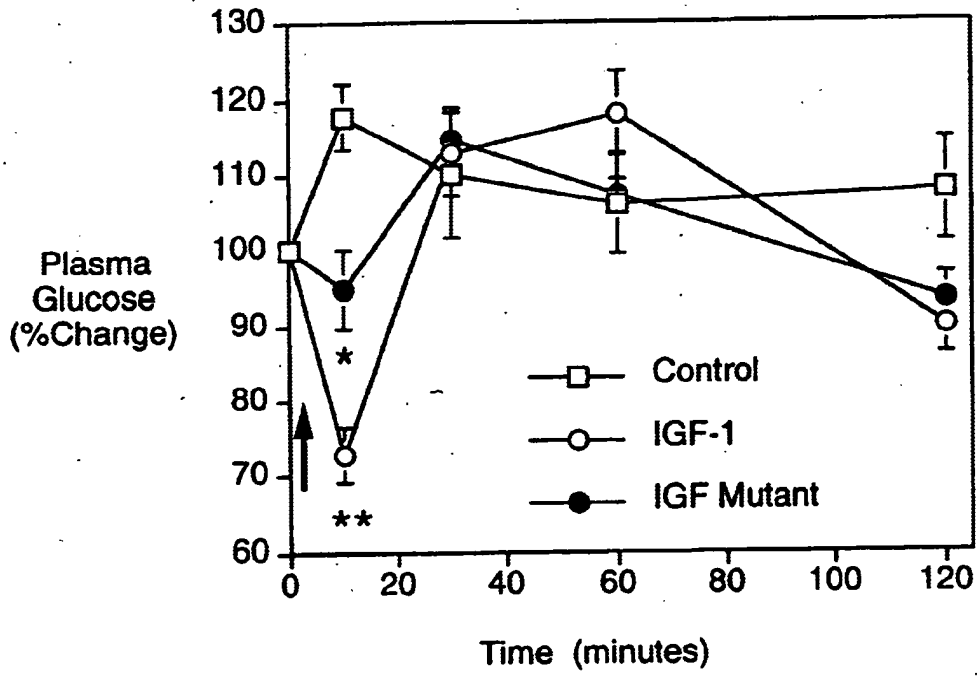


FIG. 10B

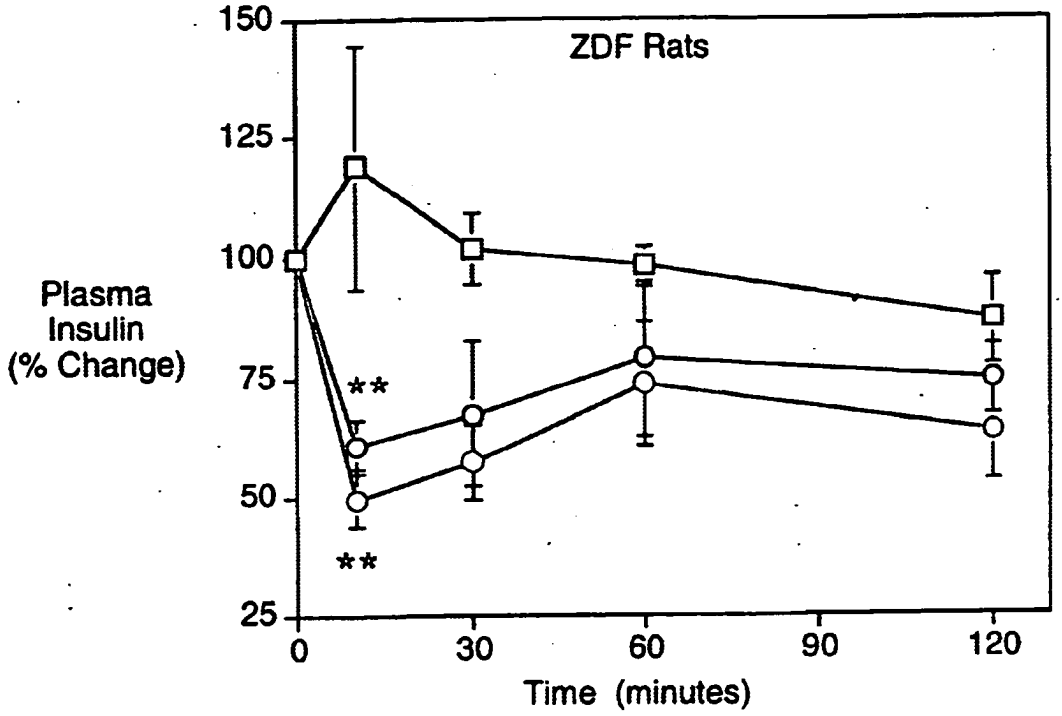


FIG. 11A

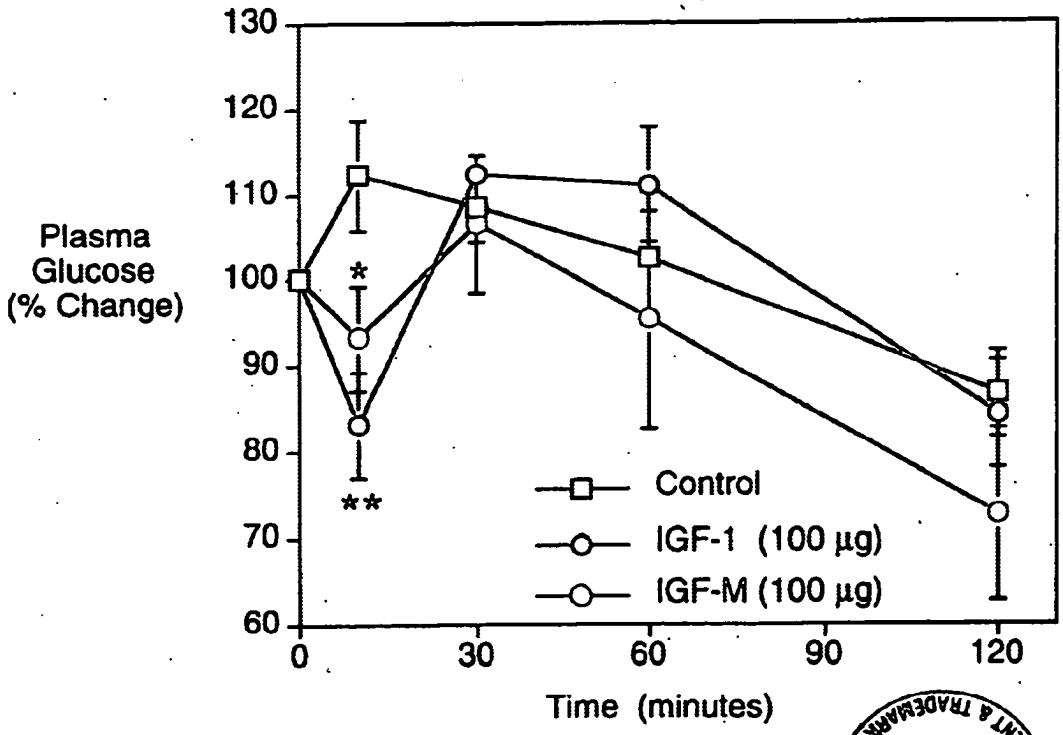


FIG. 11B

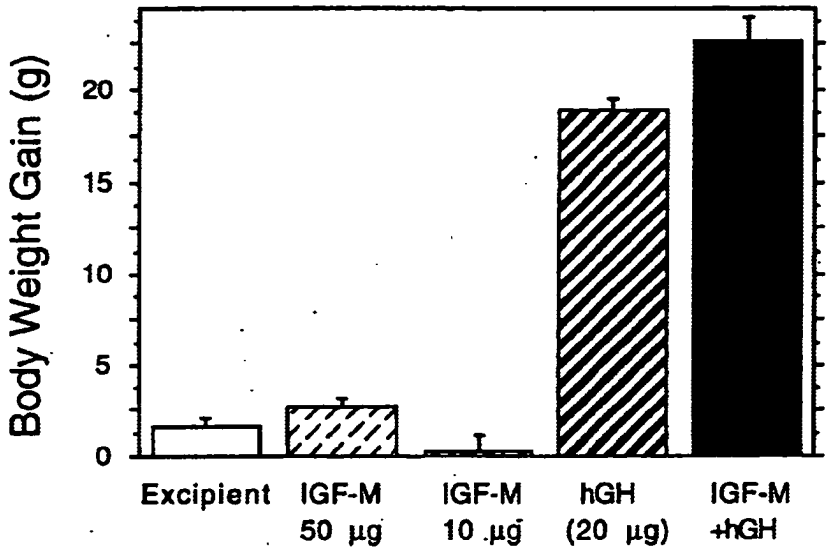


FIG. 12

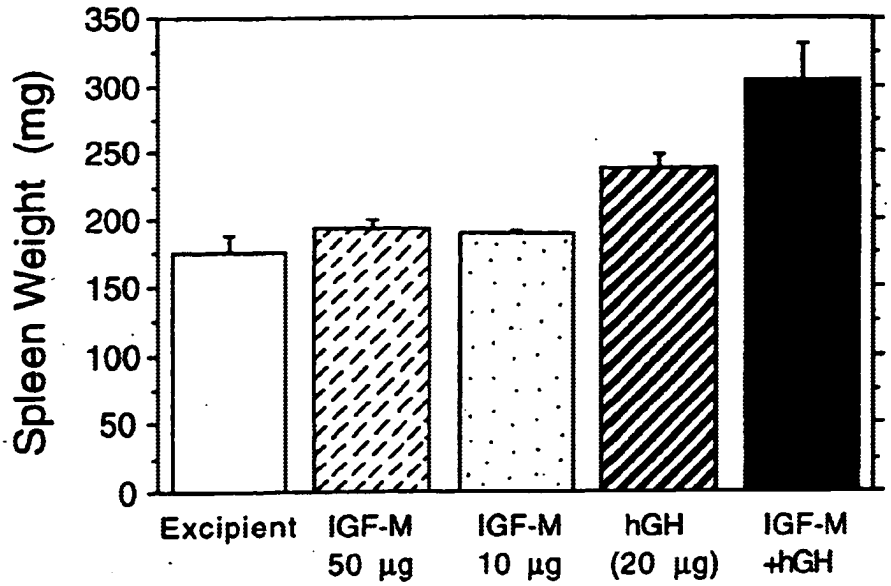


FIG. 13A

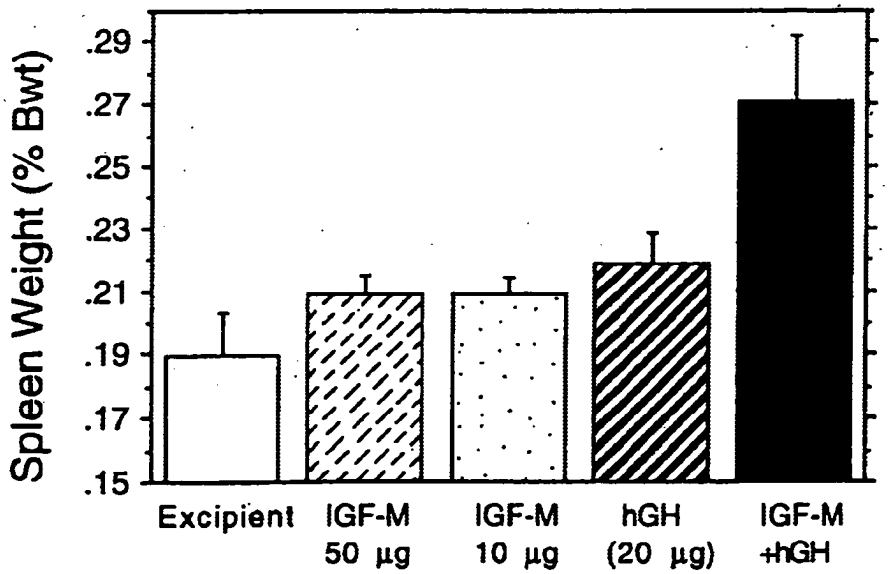


FIG. 13B

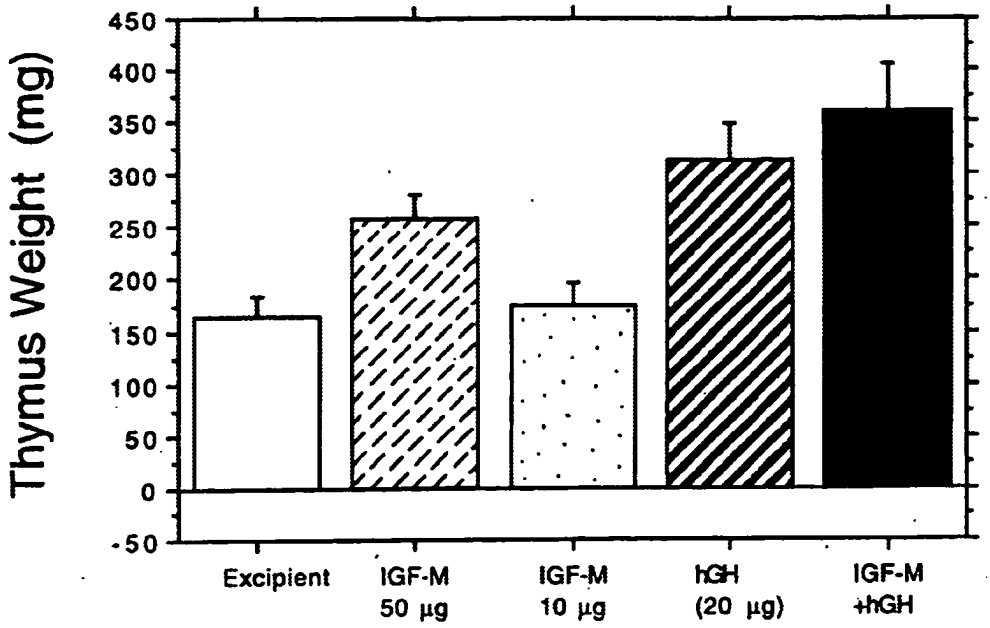


FIG. 14A

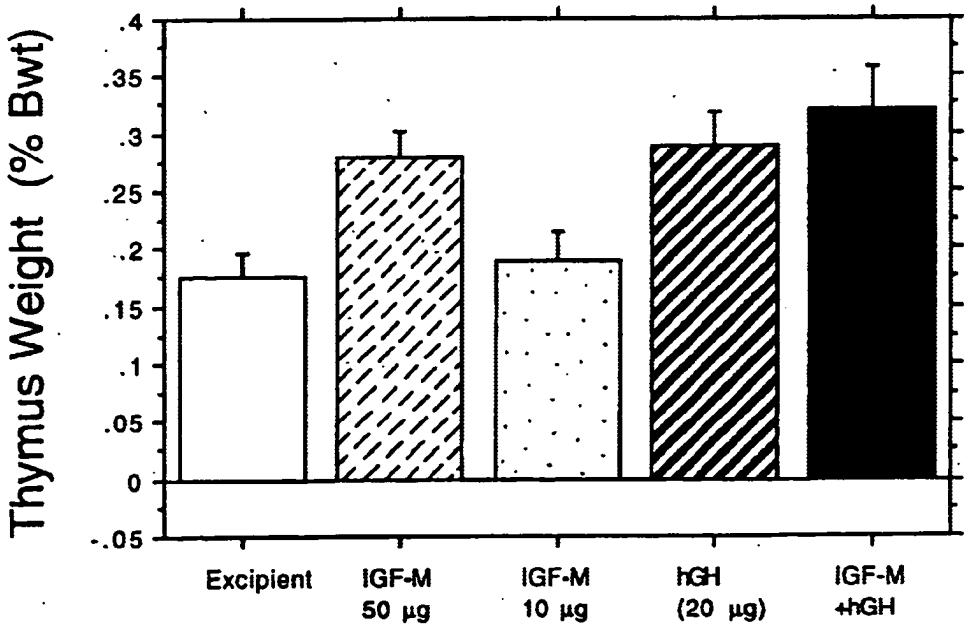


FIG. 14B

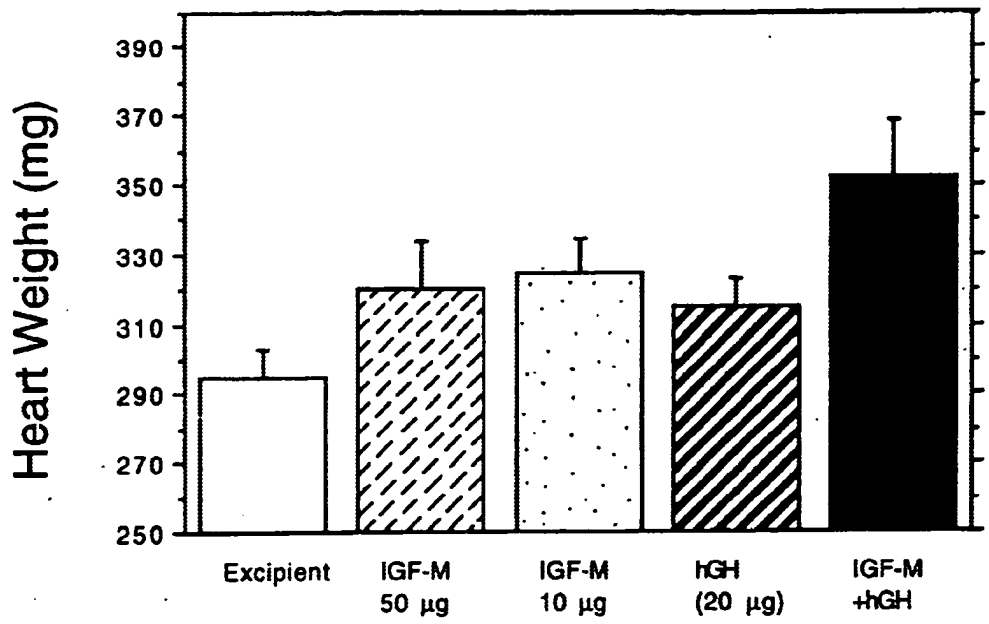


FIG. 15A

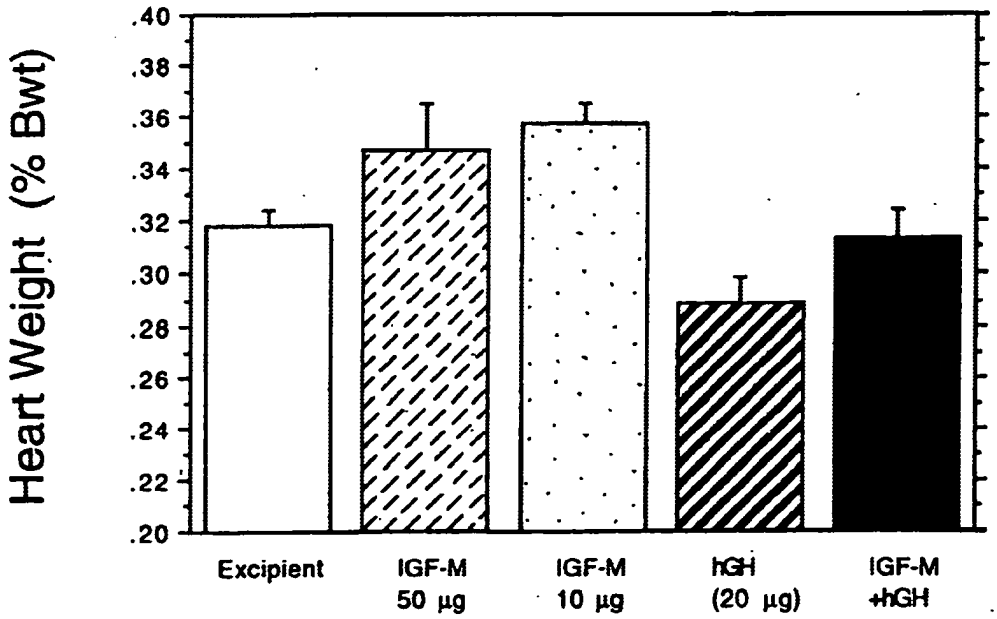


FIG. 15B

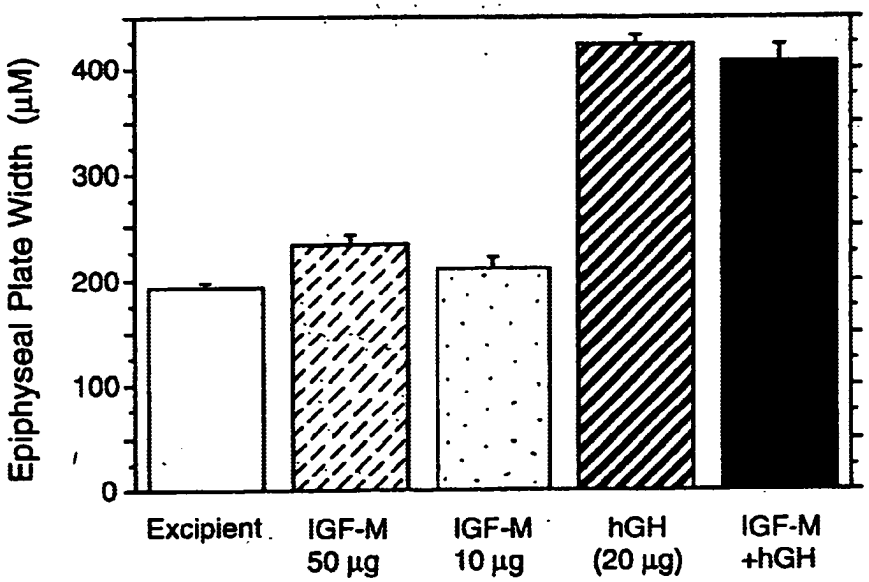


FIG. 16

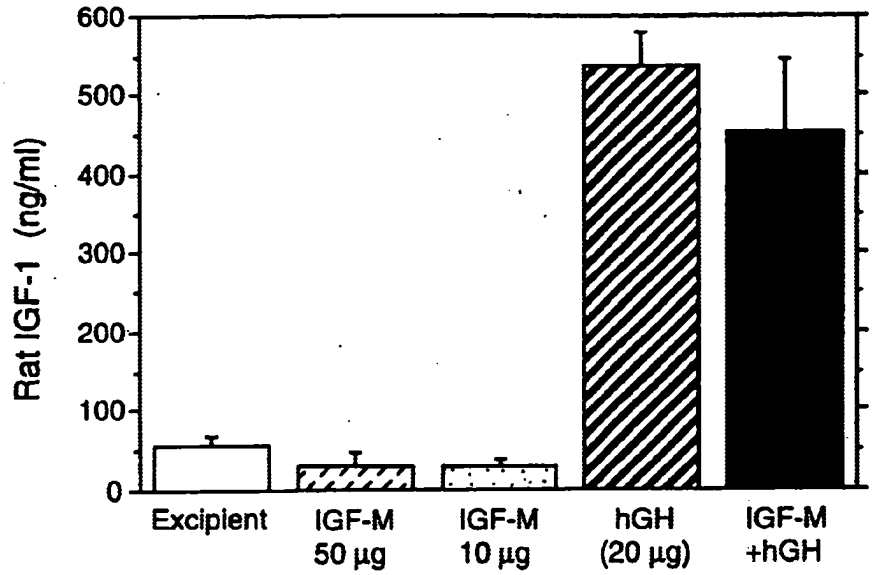


FIG. 17A

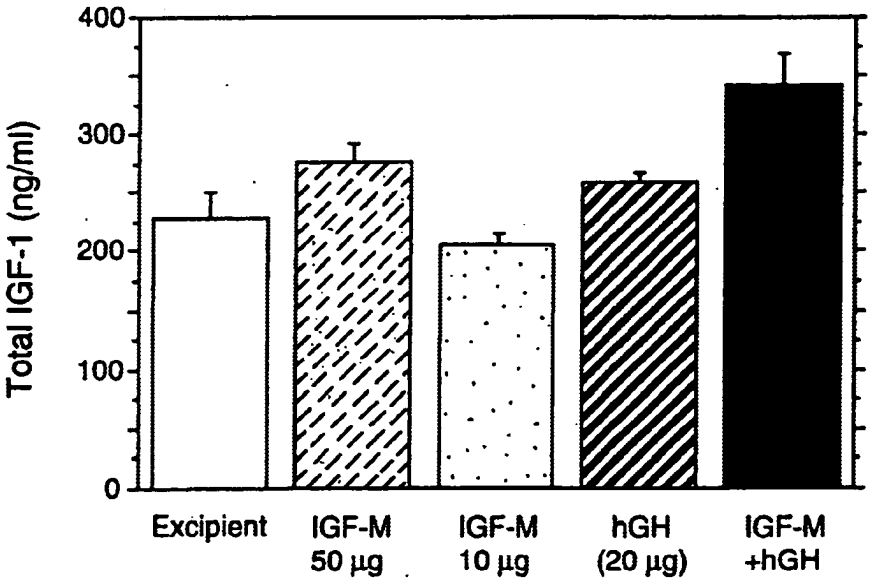


FIG. 17B

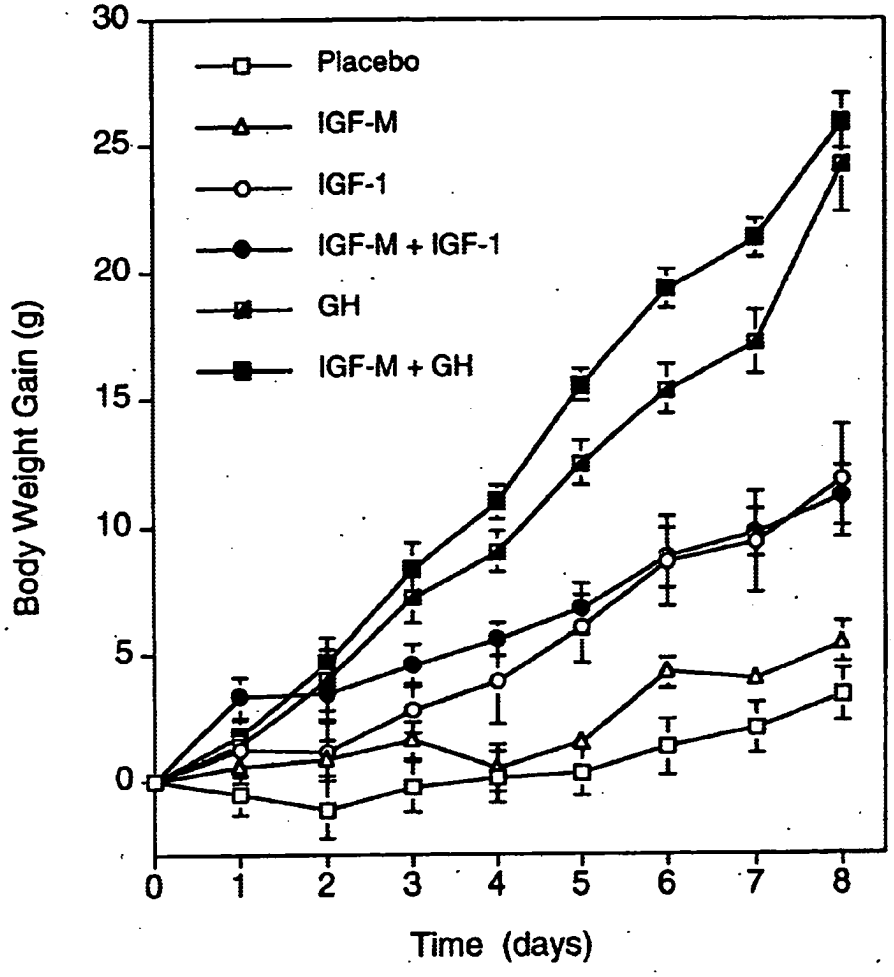


FIG. 18

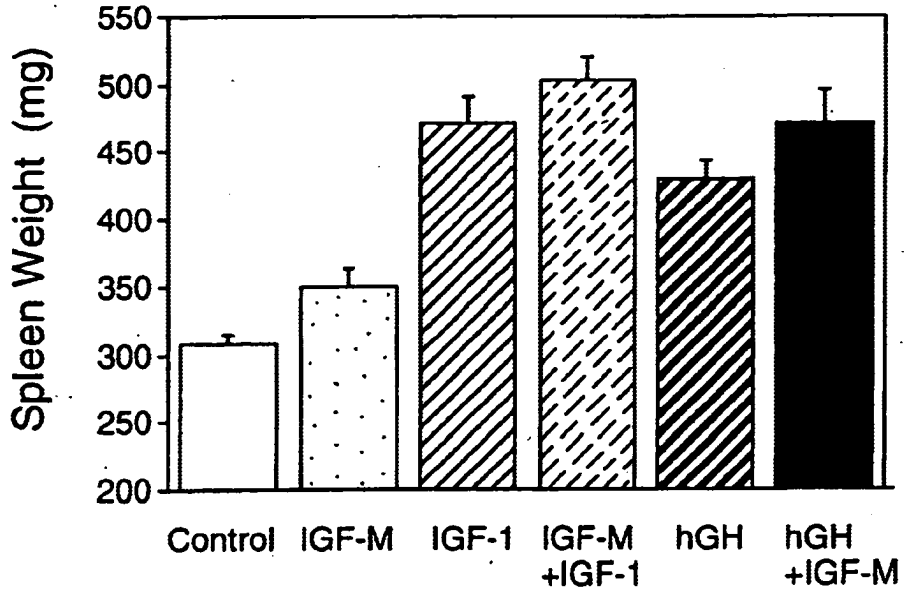


FIG. 19A

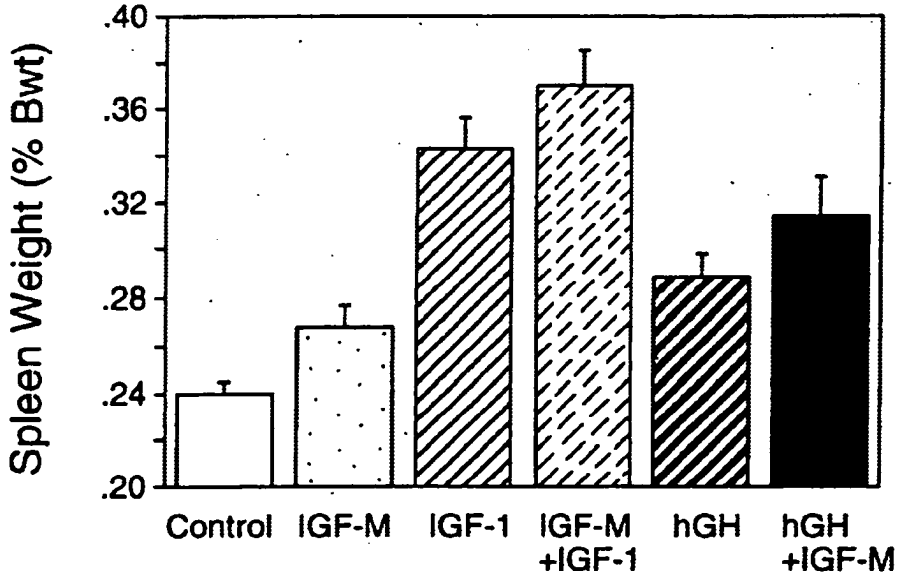


FIG. 19B

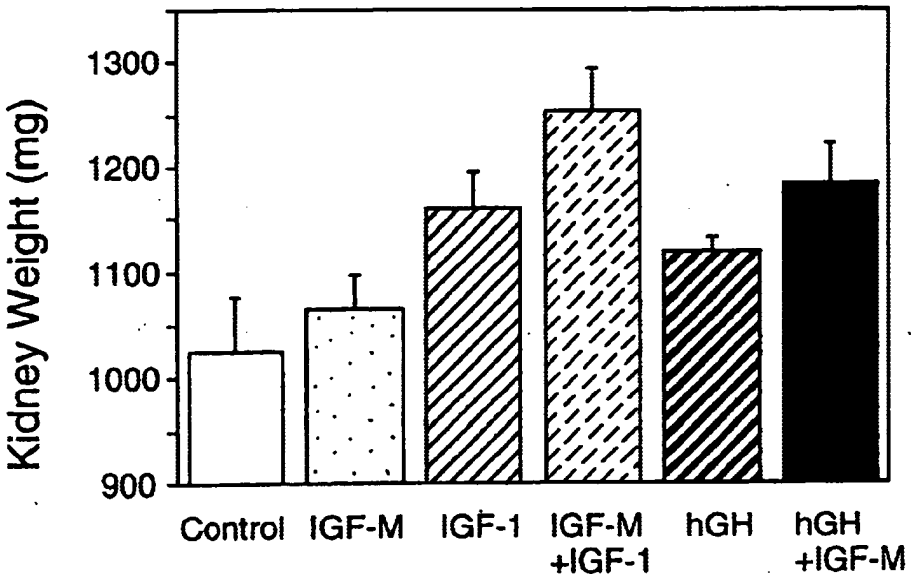


FIG. 20A

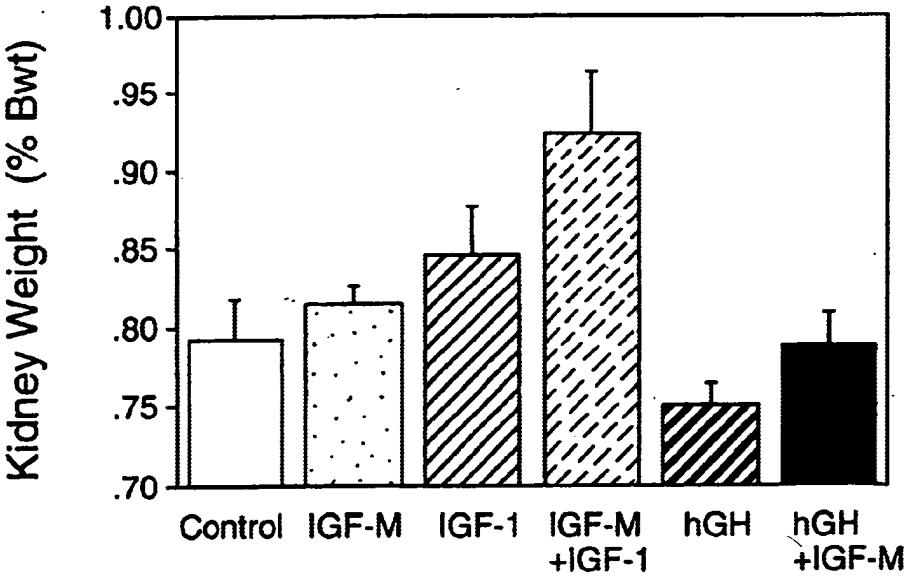


FIG. 20B

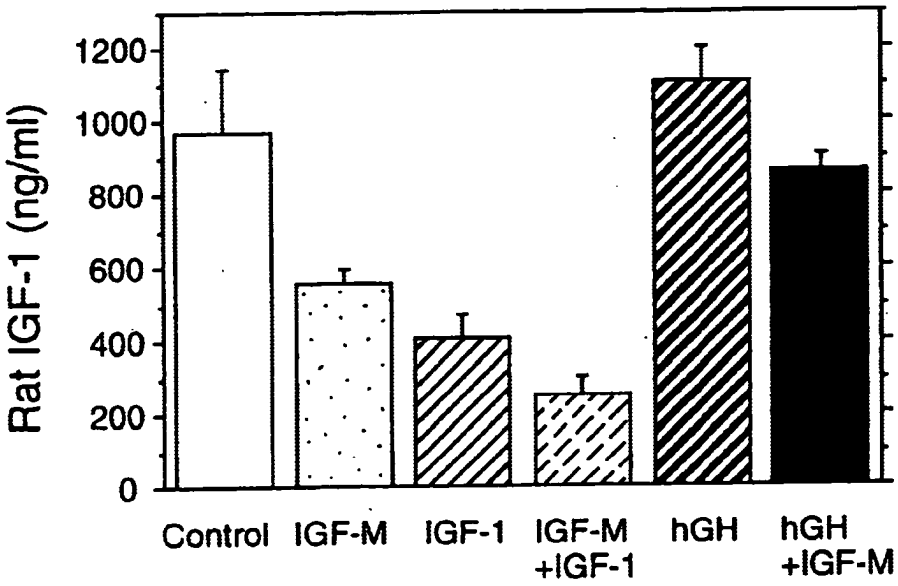


FIG. 21A

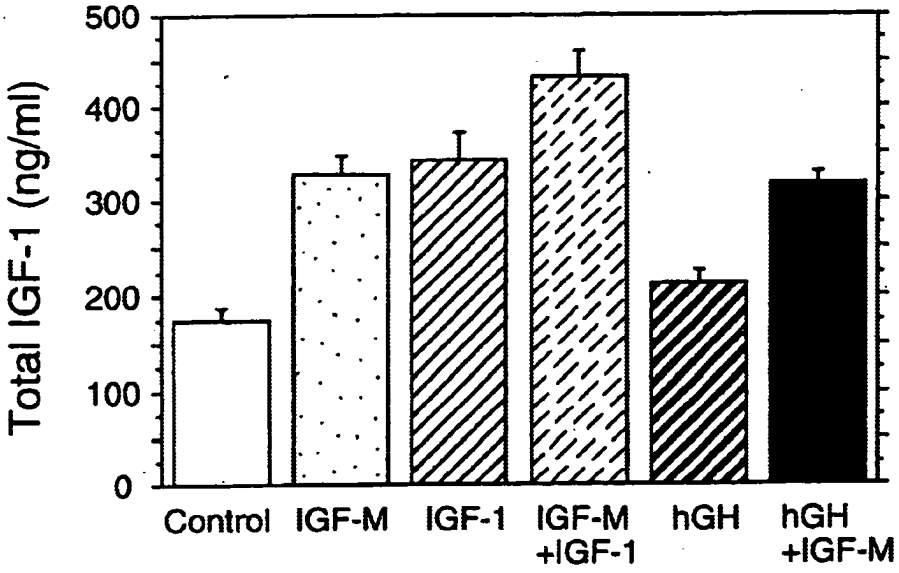


FIG. 21B

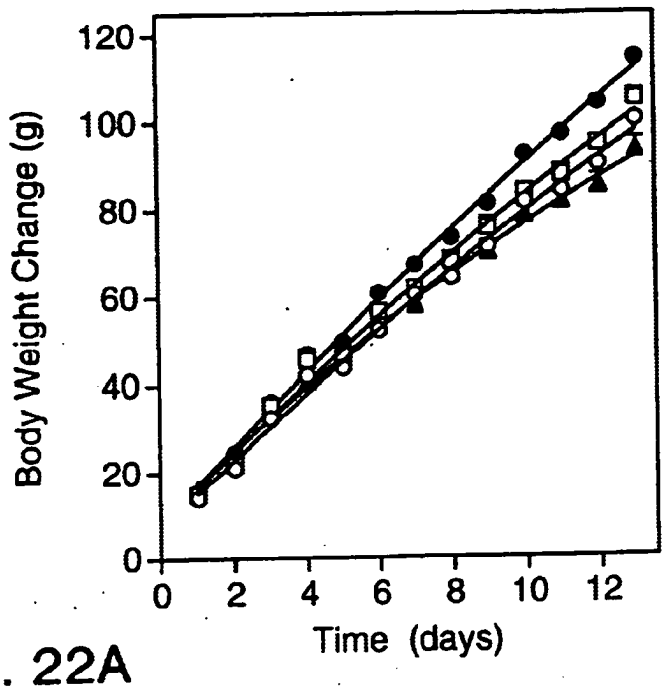


FIG. 22A

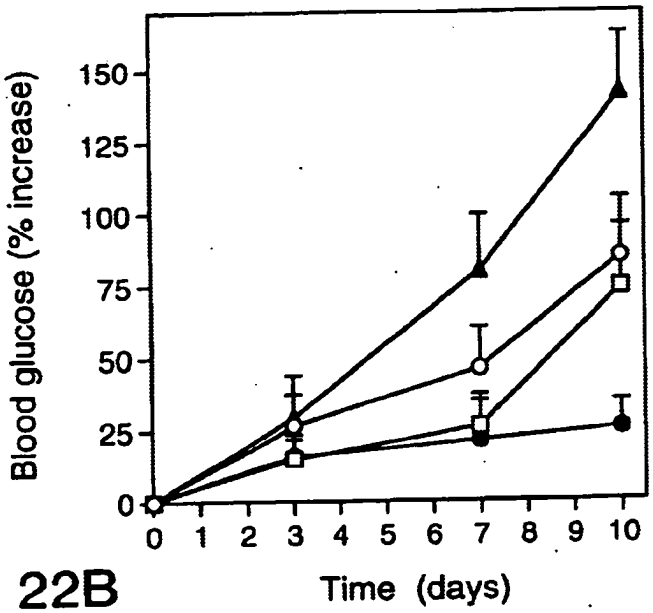


FIG. 22B

IGF-1 (150 µg, tid)

IGF Mutant (150 µg, tid)

IGF Mutant (50 µg, tid)

Excipient Control

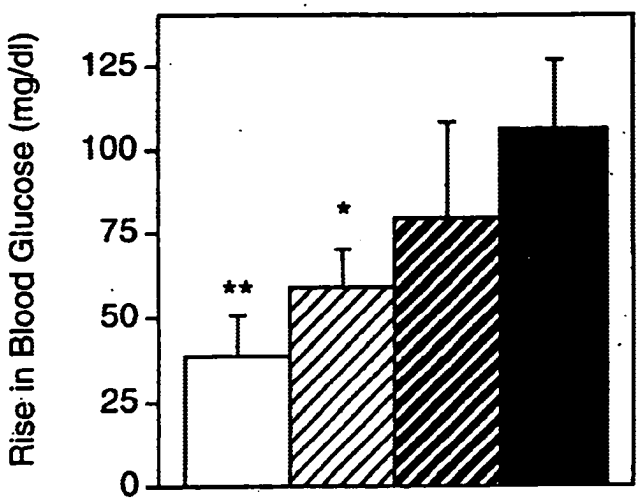


FIG. 23A

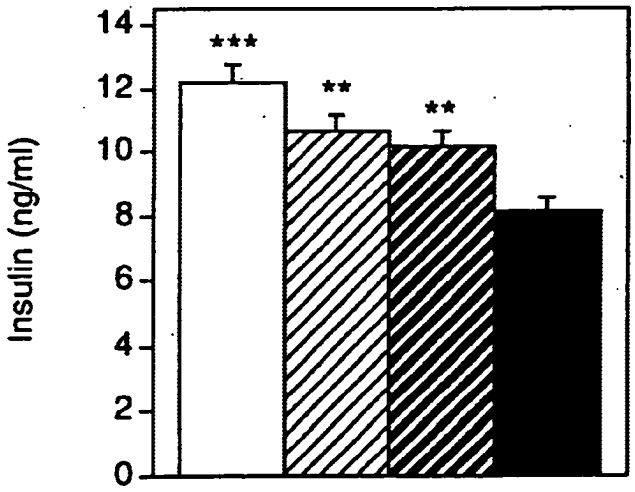
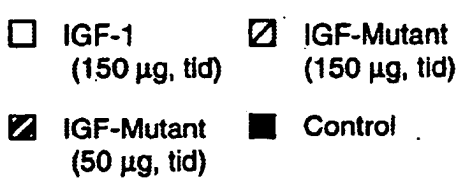


FIG. 23B



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plasmid t4.g8
length: 5140 (circular)

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       CTTAAGTTGA AGAGGTATGA AACCTATTCC TTTATGTCTG TACTTTTTAG AGTAACGACT CAACAATAAA TTCGAACGGG TTTTTCTTCT TCTCAGCTTA

   101 GAACTGTGTG CGCAGGTAGA AGCTTTGGAG ATTATCGTCA CTGCAATGCT TCGCAATATG GCGCAAAATG ACCAACAGCG GTTGATTGAT CAGGTAGAGG
       CTTGACACAC GCGTCCATCT TCGAAACCTC TAATAGCAGT GACGTTACGA AGCGTTATAC CGCGTTTTAC TGGTTGTCGC CAACTAACTA GTCCATCTCC

   201 GGGCGCTGTA CGAGGTAAAG CCCGATGCCA GCATTCCTGA CGACGATACG GAGCTGCTGC GCGATTACGT AAAGAAGTTA TTGAAGCATC CTCGTCAGTA
       CCCGCGACAT GCTCCATTTC GGGCTACGGT CGTAAGGACT GCTGCTATGC CTCGACGACG CGCTAATGCA TTTCTTCAAT AACTTCGTAG GAGCAGTCAT

   301 AAAAGTTAAT CTTTTCAACA GCTGTCATAA AGTTGTCACG GCCGAGACTT ATAGTCGCTT TGTTTTTATT TTTTAATGTA TTTGTAACTA GTACGCAAGT
       TTTTCAATTA GAAAAGTTGT CGACAGTATT TCAACAGTGC CGGCTCTGAA TATCAGCGAA ACAAAAATAA AAAATTACAT AAACATTGAT CATGCGTTCA

   401 TCACGTAAAA AGGGTATCTA GAGGTTGAGG TGATTTTATG AAAAAGAATA TCGCATTTCT TCTTGCATCT ATGTTCGTTT TTTCTATTGC TACAAATGCC
       AGTGCATTTT TCCCATAGAT CTCCAACTCC ACTAAAATAC TTTTTCTTAT AGCGTAAAGA AGAACGTAGA TACAAGCAAA AAAGATAACG ATGTTTACGG

   501 TATGCATCTG GTACCGCCAT GGCTGATCCG AACCGTTTCC GCGGTAAAGA TCTGGCAGGT TCACCAGGTG GAGGATCCGG AGGAGGCGCC GAGGGTGACG
       ATACGTAGAC CATGGCGGTA CCGACTAGGC TTGGCAAAGG CGCCATTTCT AGACCGTCCA AGTGGTCCAC CTCCTAGGCC TCCTCCGCGG CTCCCACTGC
     1       SerG lyThrAlaMe tAlaAspPro AsnArgPheA rgGlyLysAs pLeuAlaGly SerProGlyG lyGlySerGl yGlyGlyAla GluGlyAspAsp

   601 ATCCCGCAAA AGCGGCCTTT AACTCCCTGC AAGCCTCAGC GACCGAATAT ATCGGTTATG CGTGGGCGAT GGTTGTTGTC ATTGTCGGCG CAACTATCGG
       TAGGGCGTTT TCGCCGGAAA TTGAGGGACG TTCGGAGTCG CTGGCTTATA TAGCCAATAC GCACCCGCTA CCAACAACAG TAACAGCCGC GTTGATAGCC
    33   ProAlaLy sAlaAlaPhe AsnSerLeuG lnAlaSerAl aThrGluTyr IleGlyTyrA laTrpAlaMe tValValVal IleValGlyA laThrIleGly

   701 TATCAAGCTG TTTAAGAAAT TCACCTCGAA AGCAAGCTGA TAAACCGATA CAATTAAAGG CTCCTTTTGG AGCCTTTTTT TTTGGAGATT TTCAACGTGA
       ATAGTTCGAC AAATTCTTTA AGTGGAGCTT TCGTTCGACT ATTTGGCTAT GTTAATTTCC GAGGAAAACC TCGGAAAAAA AAACCTCTAA AAGTTGCACT
    66  IleLysLeu PheLysLysP heThrSerLy sAlaSer

   801 AAAAATTATT ATTCGCAATT CCTTTAGTTG TTCCTTTCTA TTCTCACTCC GCTGAAACTG TTGAAAGTTG TTTAGCAAAA CCCCATACAG AAAATTCATT
       TTTTTAATAA TAAGCGTTAA GGAAATCAAC AAGGAAAGAT AAGAGTGAGG CGACTTTGAC AACTTTCAAC AAATCGTTTT GGGGTATGTC TTTTAAGTAA

   901 TACTAACGTC TGGAAAGACG ACAAAACTTT AGATCGTTAC GCTAACTATG AGGGTTGTCT GTGGAATGCT ACAGGCGTTG TAGTTTGTAC TGGTGACGAA
       ATGATTGCAG ACCTTTCTGC TGTTTTGAAA TCTAGCAATG CGATTGATAC TCCCAACAGA CACCTTACGA TGTCCGCAAC ATCAAACATG ACCACTGCTT

  1001 ACTCAGTGTC TAGCTAGAGT GGCGGTGGCT CTGGTTCCGG TGATTTTGAT TATGAAAAGA TGGCAAACGC TAATAAGGGG GCTATGACCG AAAATGCCGA
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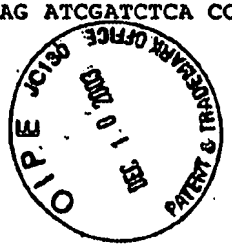

FIG. 24A

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     ACTTTTGCGC GATGTCAGAC TGCGATTTCC GTTTGAACTA AGACAGCGAT GACTAATGCC ACGACGATAG CTACCAAAGT AACCACTGCA AAGGCCGGAA

1201 GCTAATGGTA ATGGTGCTAC TGGTGATTTT GCTGGCTCTA ATTCCCAAAT GGCTCAAGTC GGTGACGGTG ATAATTCACC TTTAATGAAT AATTTCCGTC
     CGATTACCAT TACCACGATG ACCACTAAAA CGACCGAGAT TAAGGGTTTA CCGAGTTCAG CCACTGCCAC TATTAAGTGG AAATTACTTA TTAAAGGCAG

1301 AATATTTACC TTCCCTCCCT CAATCGGTTG AATGTCGCCC TTTTGTCTTT AGCGCTGGTA AACCATATGA ATTTTCTATT GATTGTGACA AAATAAACTT
     TTATAAATGG AAGGGAGGGA GTTAGCCAAC TTACAGCGGG AAAACAGAAA TCGCGACCAT TTGGTATACT TAAAAGATAA CTAACACTGT TTTATTTGAA

1401 ATTCCGTGGT GTCTTTGCGT TTCTTTTATA TGTTGCCACC TTTATGTATG TATTTTCTAC GTTTGCTAAC ATACTGCGTA ATAAGGAGTC TTAATCATGC
     TAAGGCACCA CAGAAACGCA AAGAAAATAT ACAACGGTGG AAATACATAC ATAAAAGATG CAAACGATTG TATGACGCAT TATTCCTCAG AATTAGTACG

3201 ACTCAAAGGC GGTAATACGG TTATCCACAG AATCAGGGGA TAACGCAGGA AAGAACATGT GAGCAAAAGG CCAGCAAAAG GCCAGGAACC GTAAAAAGGC
     TGAGTTTCCG CCATTATGCC AATAGGTGTC TTAGTCCCCT ATTGCGTCCT TTCTTGTACA CTCGTTTTCC GGTCGTTTTC CGGTCCTTGG CATTTTTCCG

3301 CGCGTTGCTG GCGTTTTTCC ATAGGCTCCG CCCCCCTGAC GAGCATCACA AAAATCGACG CTCAAGTCAG AGGTGGCGAA ACCCGACAGG ACTATAAAGA
     GCGCAACGAC CGCAAAAAGG TATCCGAGGC GGGGGGACTG CTCGTAGTGT TTTTAGCTGC GAGTTCAGTC TCCACCGCTT TGGGCTGTCC TGATATTTCT

3401 TACCAGGCGT TTCCCCCTGG AAGCTCCCTC GTGCGCTCTC CTGTTCCGAC CCTGCCGCTT ACCGGATACC TGTCCGCCTT TCTCCCTTCG GGAAGCGTGG
     ATGGTCCGCA AAGGGGGACC TTCGAGGGAG CACGCGAGAG GACAAGGCTG GGACGGCGAA TGGCCTATGG ACAGGCGGAA AGAGGGAAGC CCTTCGCACC

3501 CGCTTTCTCA TAGCTCACGC TGTAGGTATC TCAGTTCGGT GTAGGTCGTT CGCTCCAAGC TGGGCTGTGT GCACGAACCC CCCGTTCAGC CCGACCGCTG
     GCGAAAGAGT ATCGAGTGCG ACATCCATAG AGTCAAGCCA CATCCAGCAA GCGAGGTTCG ACCCGACACA CGTGCTTGGG GGGCAAGTCG GGCTGGCGAC

3601 CGCCTTATCC GGTAACTATC GTCTTGAGTC CAACCCGGTA AGACACGACT TATCGCCACT GGCAGCAGCC ACTGGTAACA GGATTAGCAG AGCGAGGTAT
     GCGGAATAGG CCATTGATAG CAGAACTCAG GTTGGGCCAT TCTGTGCTGA ATAGCGGTGA CCGTCGTCGG TGACCATTGT CCTAATCGTC TCGCTCCATA

3701 GTAGGCGGTG CTACAGAGTT CTTGAAGTGG TGGCCTAACT ACGGCTACAC TAGAAGGACA GTATTTGGTA TCTGCGCTCT GCTGAAGCCA GTTACCTTCG
     CATCCGCCAC GATGTCTCAA GAACTTCACC ACCGGATTGA TGCCGATGTG ATCTTCCTGT CATAAACCAT AGACGCGAGA CGACTTCGGT CAATGGAAGC

3801 GAAAAAGAGT TGGTAGCTCT TGATCCGGCA AACAAACCAC CGCTGGTAGC GGTGGTTTTT TTGTTTGCAA GCAGCAGATT ACGCGCAGAA AAAAAGGATC
     CTTTTTCTCA ACCATCGAGA ACTAGGCCGT TTGTTTGGTG GCGACCATCG CCACCAAAAA AACAAACGTT CGTCGTCTAA TGCGCGTCTT TTTTTCCTAG

3901 TCAAGAAGAT CCTTTGATCT TTTCTACGGG GTCTGACGCT CAGTGGAACG AAAACTCACG TTAAGGGATT TTGGTCATGA GATTATCAAA AAGGATCTTC
     AGTTCTTCTA GGAAACTAGA AAAGATGCCC CAGACTGCGA GTCACCTTGC TTTTGAGTGC AATTCCCTAA AACCAGTACT CTAATAGTTT TTCCTAGAAG

4001 ACCTAGATCC TTTTAAATTA AAAATGAAGT TTTAAATCAA TCTAAAGTAT ATATGAGTAA ACTTGGTCTG ACAGTTACCA ATGCTTAATC AGTGAGGCAC
     TGGATCTAGG AAAATTTAAT TTTTACTTCA AAATTTAGTT AGATTTCATA TATACTCATT TGAACCAGAC TGTCAATGGT TACGAATTAG TCACTCCGTG
```

FIG. 24B

```
4101 CTATCTCAGC GATCTGTCTA TTTCGTTCAT CCATAGTTGC CTGACTCCCC GTCGTGTAGA TAACTACGAT ACGGGAGGGC TTACCATCTG GCCCCAGTGC
     GATAGAGTCG CTAGACAGAT AAAGCAAGTA GGTATCAACG GACTGAGGGG CAGCACATCT ATTGATGCTA TGCCCTCCCG AATGGTAGAC CGGGGTCACG

4201 TGCAATGATA CCGCGAGACC CACGCTCACC GGCTCCAGAT TTATCAGCAA TAAACCAGCC AGCCGGAAGG GCCGAGCGCA GAAGTGGTCC TGCAACTTTA
     ACGTTACTAT GGCGCTCTGG GTGCGAGTGG CCGAGGTCTA AATAGTCGTT ATTTGGTCGG TCGGCCTTCC CGGCTCGCGT CTTCACCAGG ACGTTGAAAT

4301 TCCGCCTCCA TCCAGTCTAT TAATTGTTGC CGGGAAGCTA GAGTAAGTAG TTCGCCAGTT AATAGTTTGC GCAACGTTGT TGCCATTGCT GCAGGCATCG
     AGGCGGAGGT AGGTCAGATA ATTAACAACG GCCCTTCGAT CTCATTCATC AAGCGGTCAA TTATCAAACG CGTTGCAACA ACGGTAACGA CGTCCGTAGC

4401 TGGTGTCACG CTCGTCGTTT GGTATGGCTT CATTCAGCTC CGGTTCCCAA CGATCAAGGC GAGTTACATG ATCCCCCATG TTGTGCAAAA AAGCGGTTAG
     ACCACAGTGC GAGCAGCAAA CCATACCGAA GTAAGTCGAG GCCAAGGGTT GCTAGTTCCG CTCAATGTAC TAGGGGGTAC AACACGTTTT TTCGCCAATC

4501 CTCCTTCGGT CCTCCGATCG TTGTCAGAAG TAAGTTGGCC GCAGTGTTAT CACTCATGGT TATGGCAGCA CTGCATAATT CTCTTACTGT CATGCCATCC
     GAGGAAGCCA GGAGGCTAGC AACAGTCTTC ATTCAACCGG CGTCACAATA GTGAGTACCA ATACCGTCGT GACGTATTAA GAGAATGACA GTACGGTAGG

4601 GTAAGATGCT TTTCTGTGAC TGGTGAGTAC TCAACCAAGT CATTCTGAGA ATAGTGTATG CGGCGACCGA GTTGCTCTTG CCCGGCGTCA ACACGGGATA
     CATTCTACGA AAAGACACTG ACCACTCATG AGTTGGTTCA GTAAGACTCT TATCACATAC GCCGCTGGCT CAACGAGAAC GGGCCGCAGT TGTGCCCTAT

4701 ATACCGCGCC ACATAGCAGA ACTTTAAAAG TGCTCATCAT TGGAAAACGT TCTTCGGGGC GAAAACTCTC AAGGATCTTA CCGCTGTTGA GATCCAGTTC
     TATGGCGCGG TGTATCGTCT TGAAATTTTC ACGAGTAGTA ACCTTTTGCA AGAAGCCCCG CTTTTGAGAG TTCCTAGAAT GGCGACAACT CTAGGTCAAG

4801 GATGTAACCC ACTCGTGCAC CCAACTGATC TTCAGCATCT TTTACTTTCA CCAGCGTTTC TGGGTGAGCA AAAACAGGAA GGCAAAATGC CGCAAAAAAG
     CTACATTGGG TGAGCACGTG GGTTGACTAG AAGTCGTAGA AAATGAAAGT GGTCGCAAAG ACCCACTCGT TTTTGTCCTT CCGTTTTACG GCGTTTTTTC

4901 GGAATAAGGG CGACACGGAA ATGTTGAATA CTCATACTCT TCCTTTTTCA ATATTATTGA AGCATTTATC AGGGTTATTG TCTCATGAGC GGATACATAT
     CCTTATTCCC GCTGTGCCTT TACAACTTAT GAGTATGAGA AGGAAAAAGT TATAATAACT TCGTAAATAG TCCCAATAAC AGAGTACTCG CCTATGTATA

5001 TTGAATGTAT TTAGAAAAAT AAACAAATAG GGGTTCCGCG CACATTTCCC CGAAAAGTGC CACCTGACGT CTAAGAAACC ATTATTATCA TGACATTAAC
     AACTTACATA AATCTTTTTA TTTGTTTATC CCCAAGGCGC GTGTAAAGGG GCTTTTCACG GTGGACTGCA GATTCTTTGG TAATAATAGT ACTGTAATTG

5101 CTATAAAAAT AGGCGTATCA CGAGGCCCTT TCGTCTTCAA
     GATATTTTTA TCCGCATAGT GCTCCGGGAA AGCAGAAGTT
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FIG. 24C

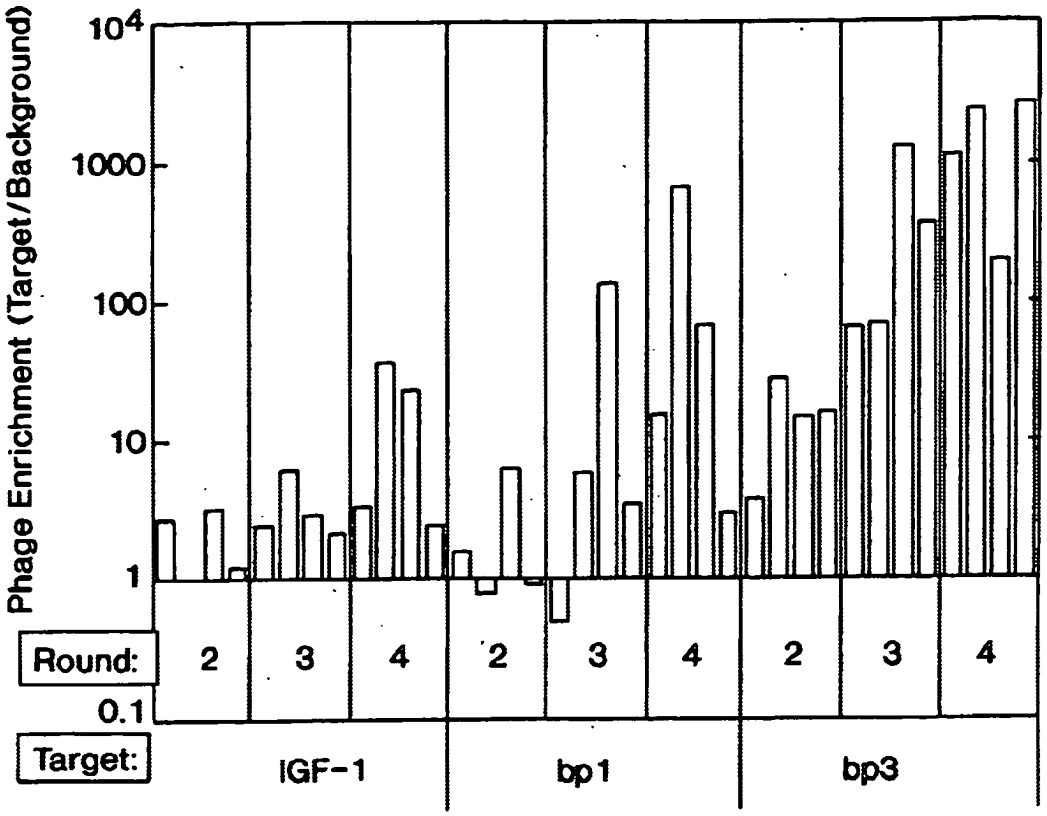

FIG. 25

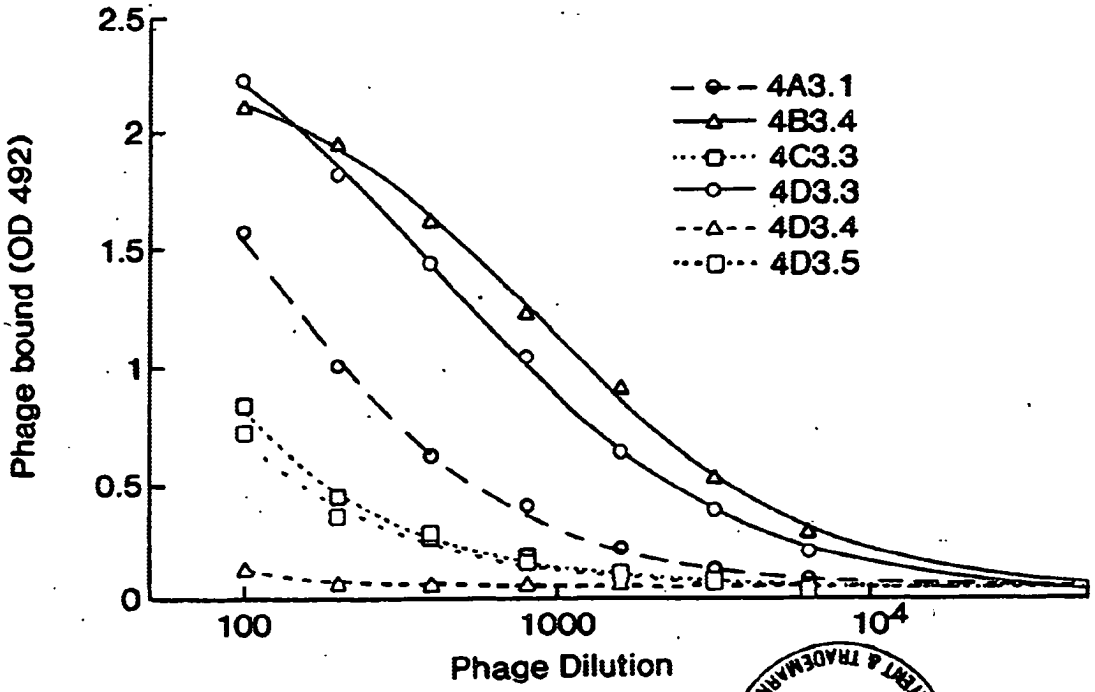

FIG. 26

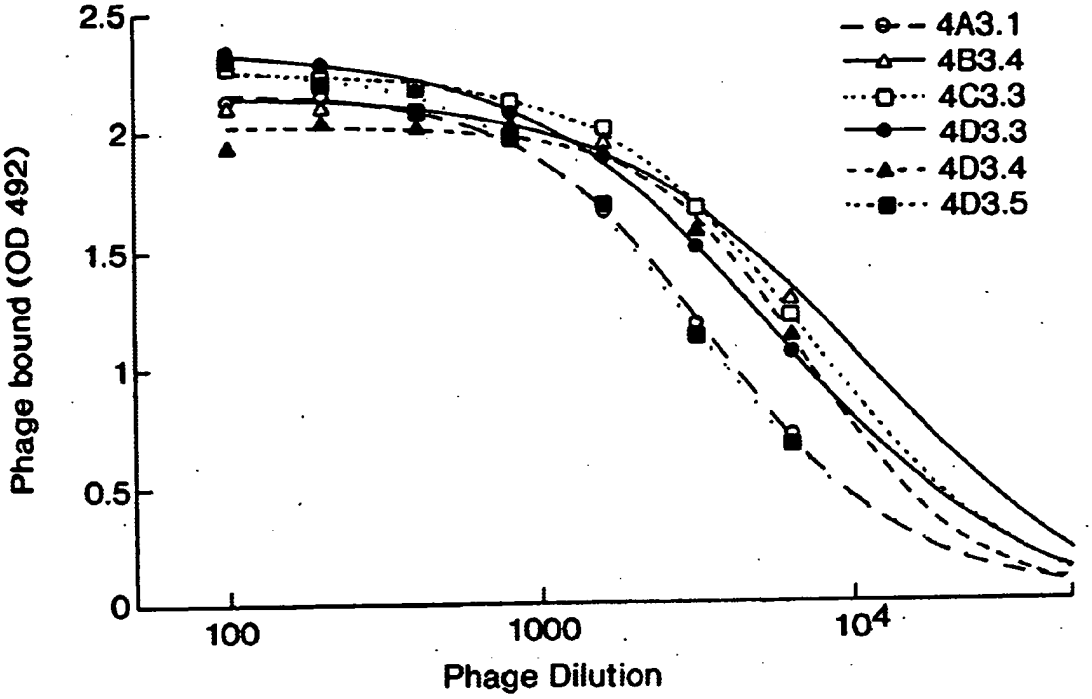

FIG. 27

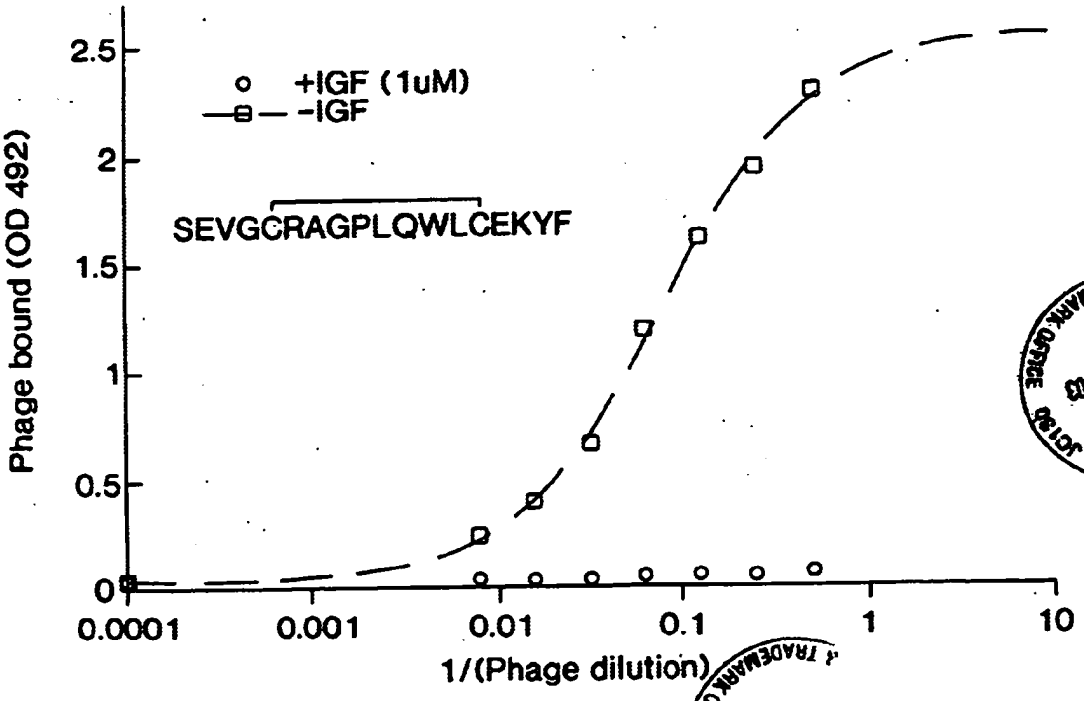

FIG. 28

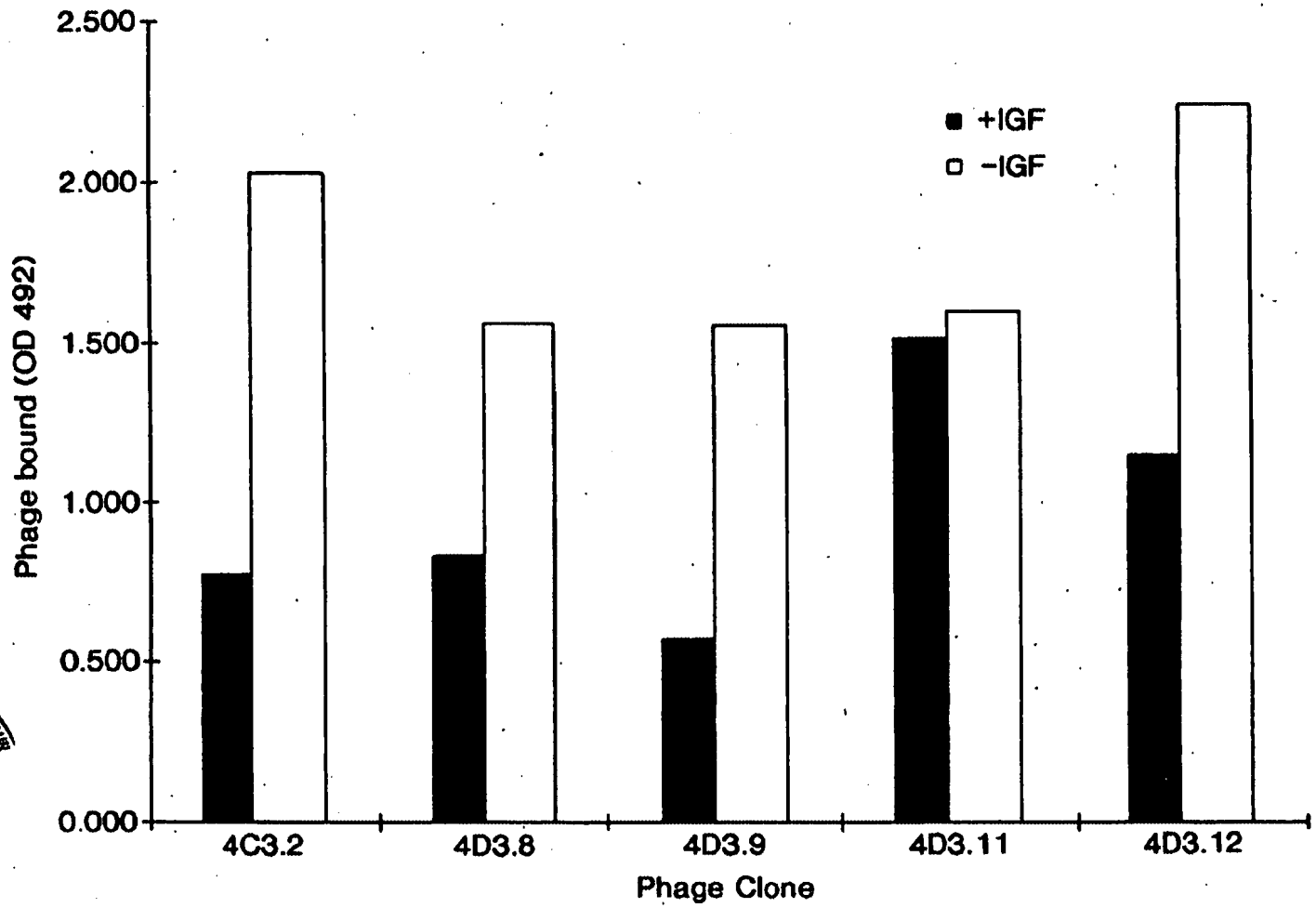

FIG. 29

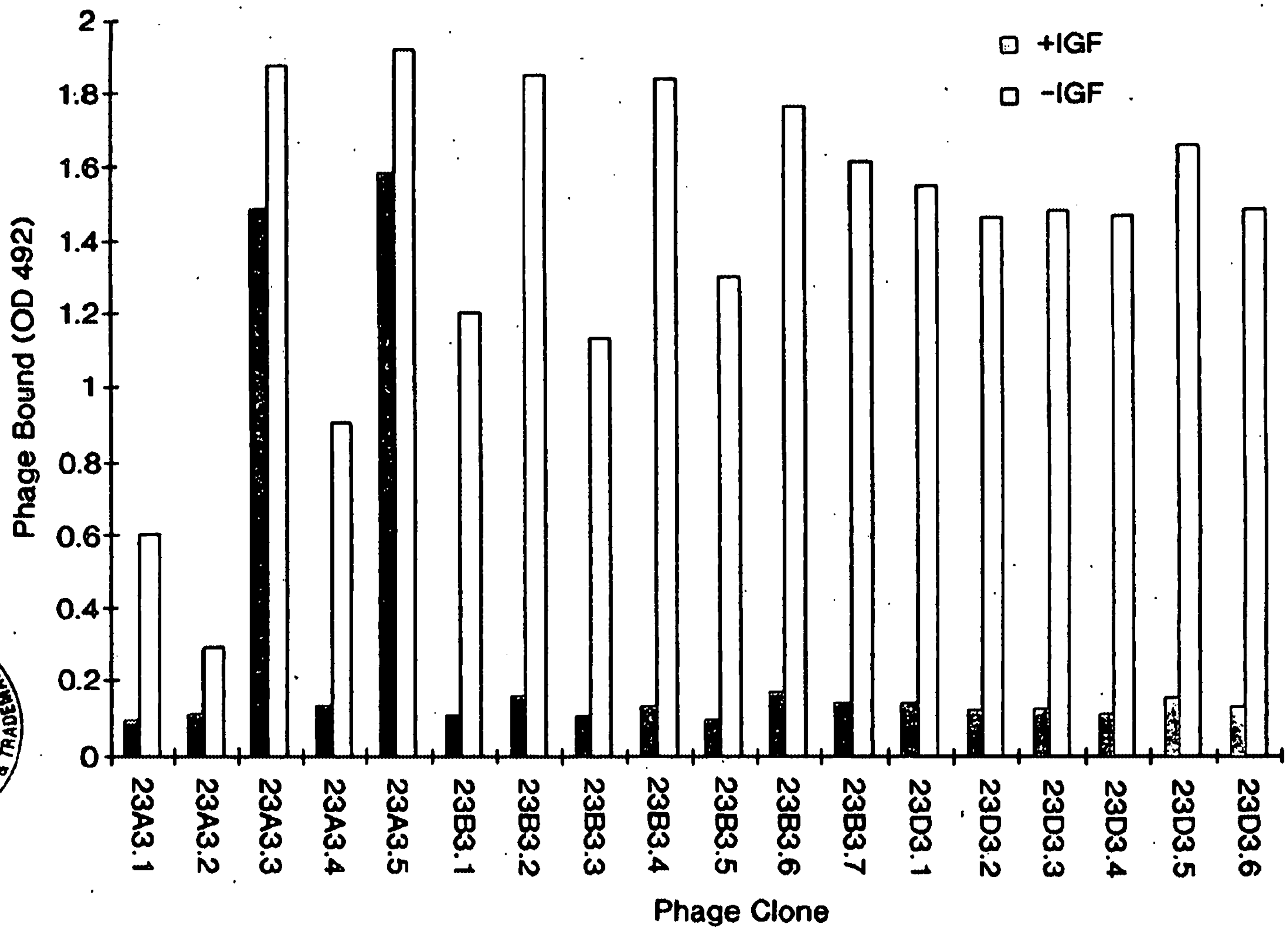

FIG. 30

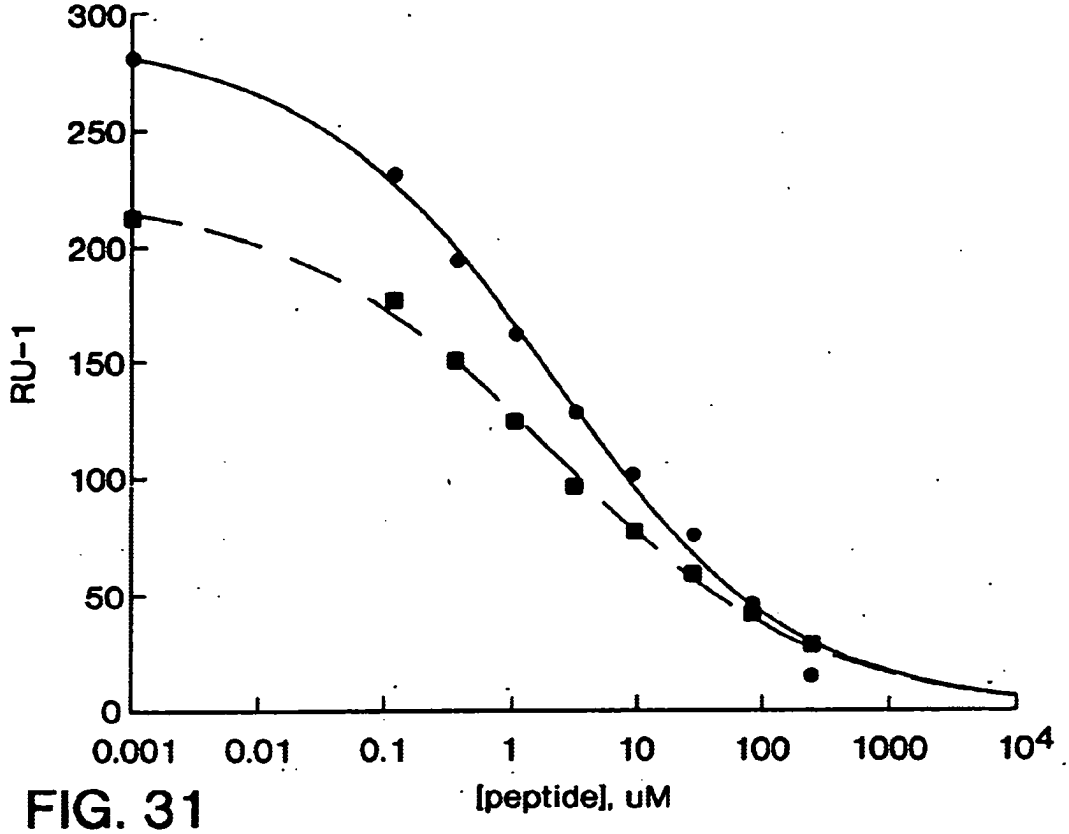

FIG. 31

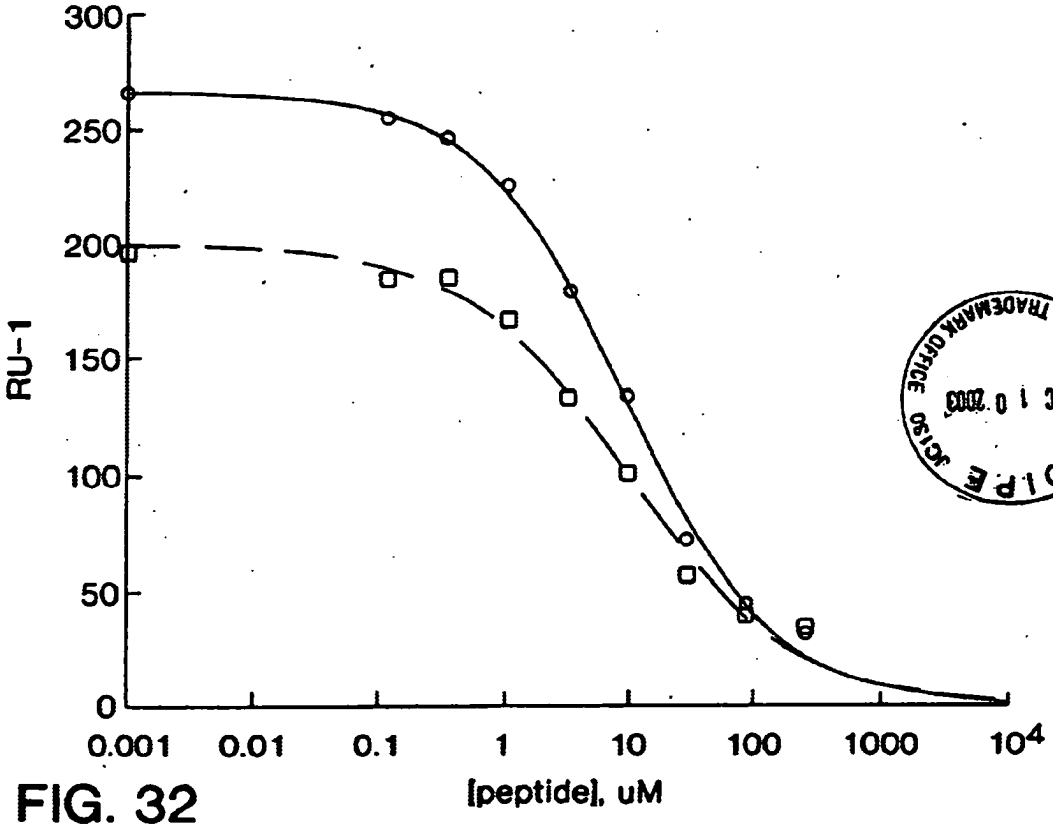

FIG. 32

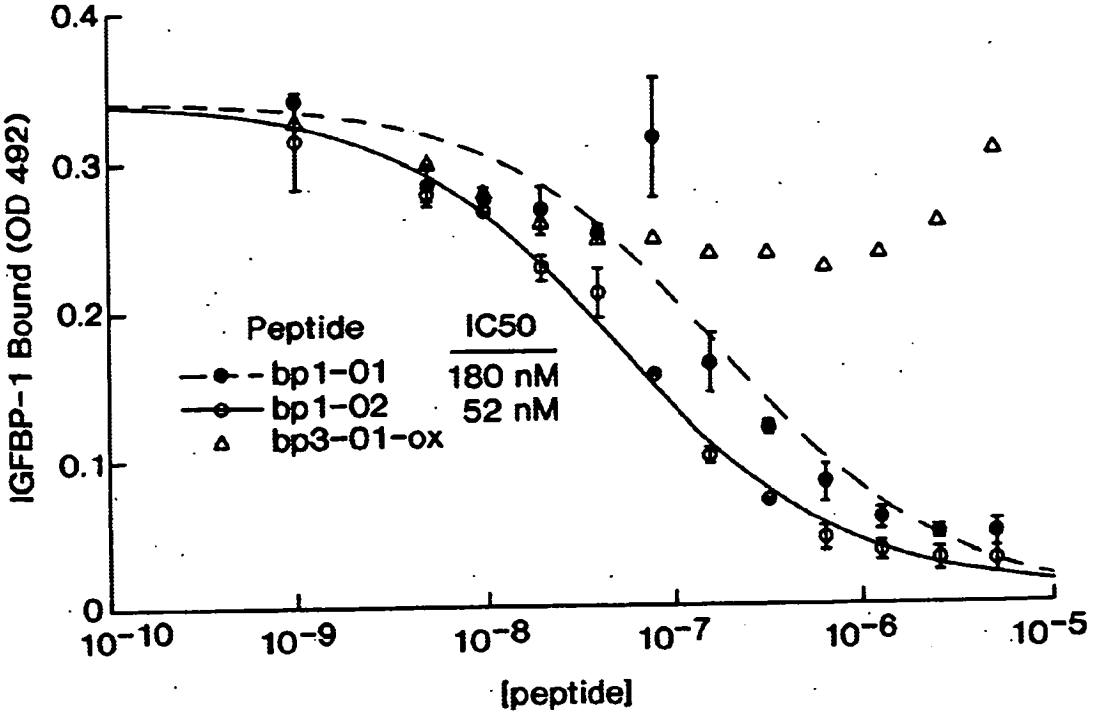

FIG. 33

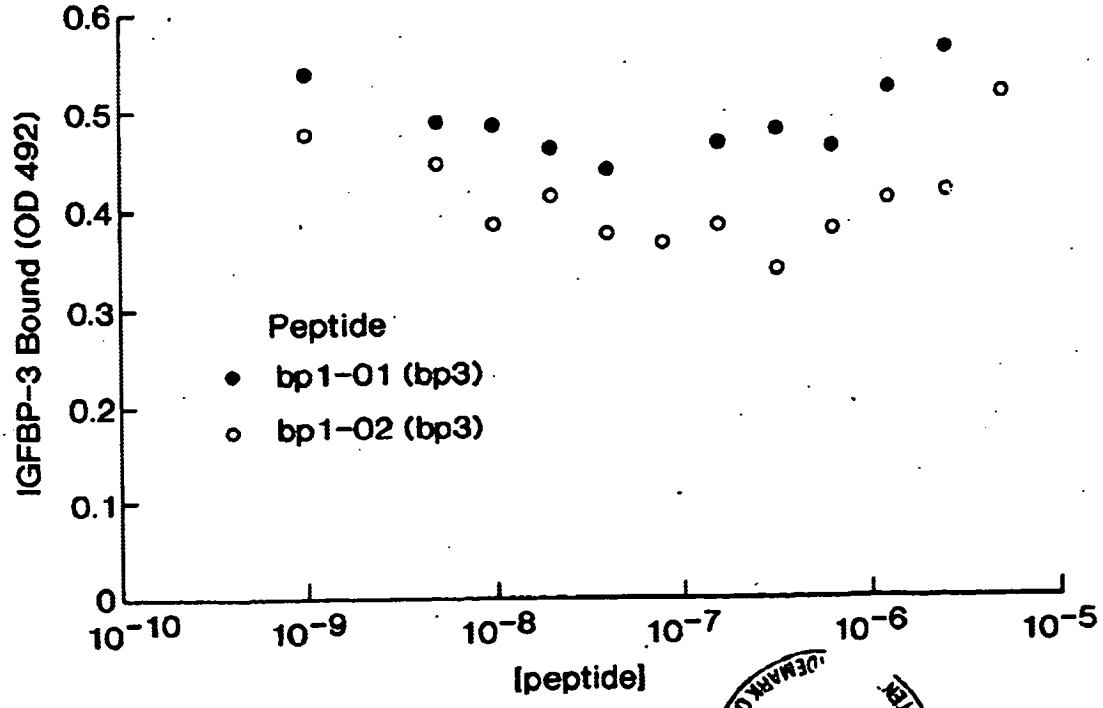

FIG. 34

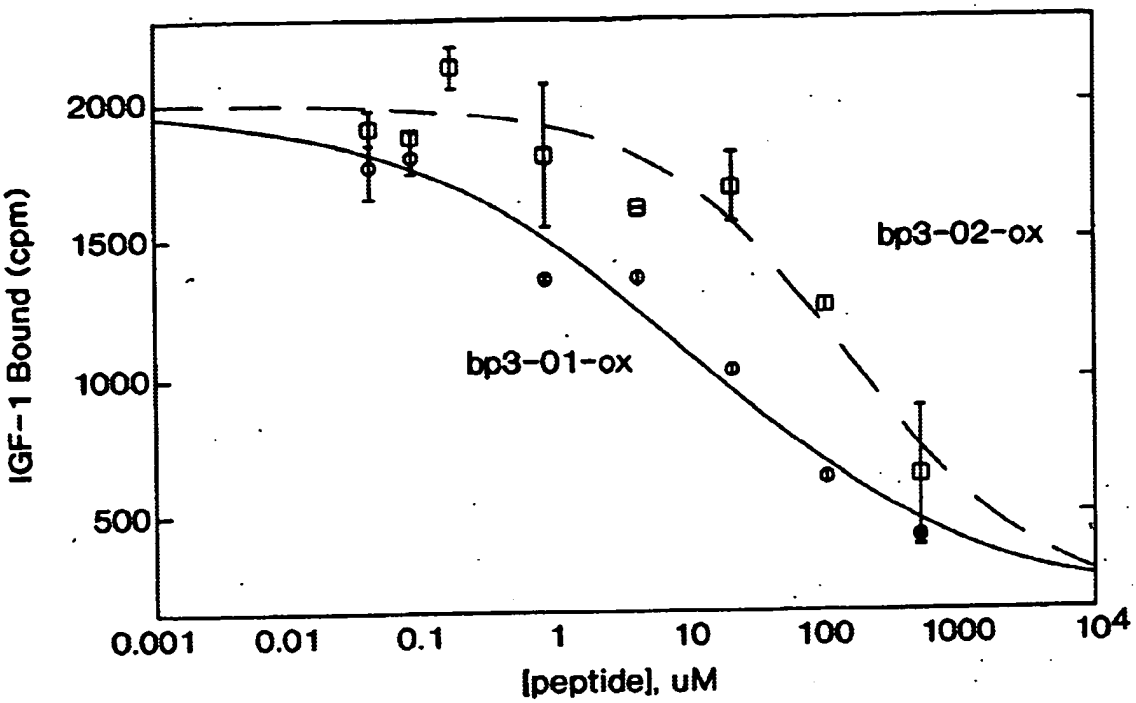

FIG. 35

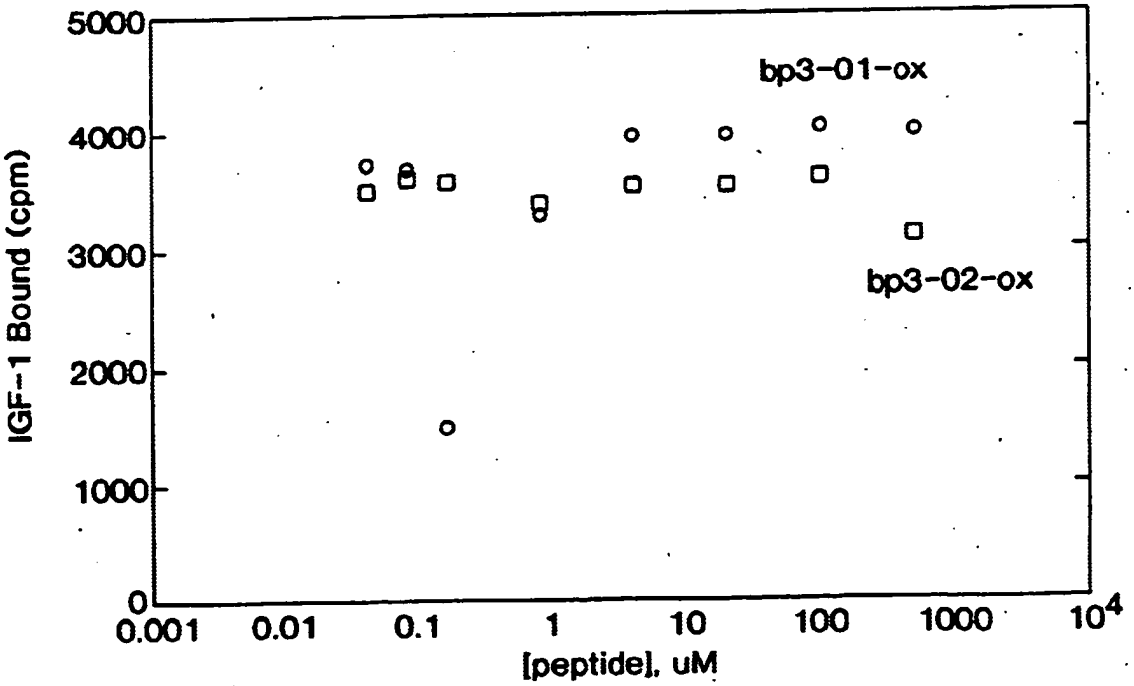

FIG. 36

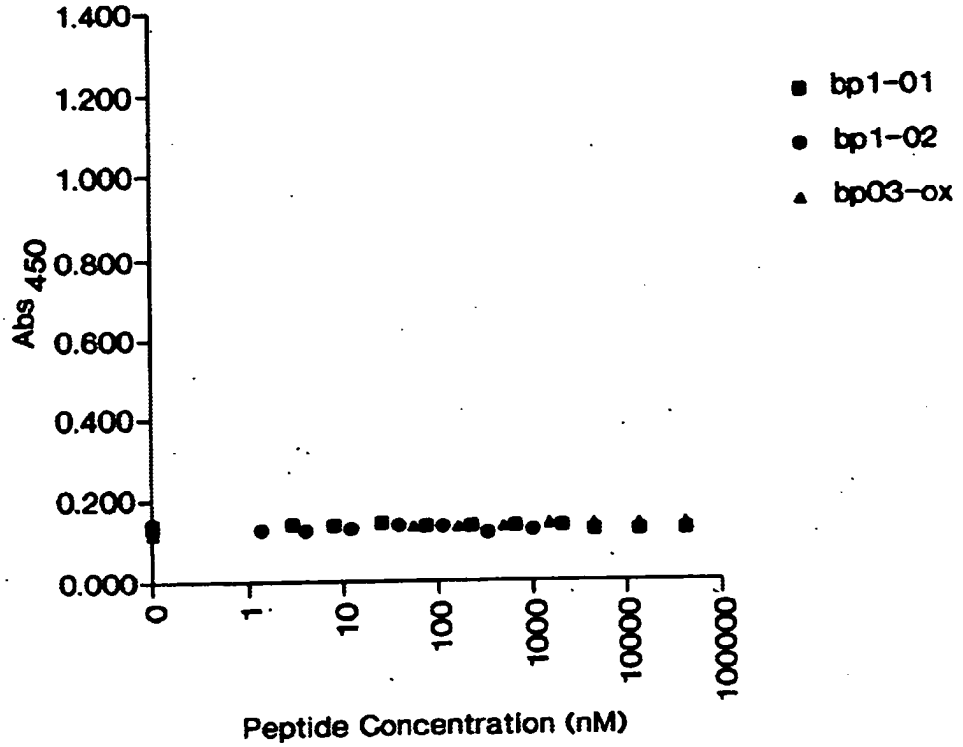

FIG. 37A

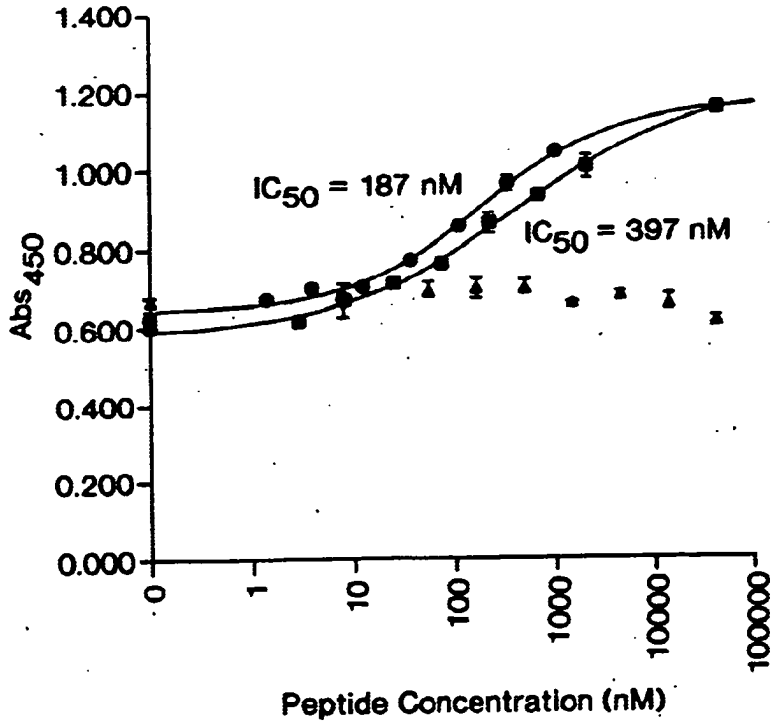

FIG. 37B

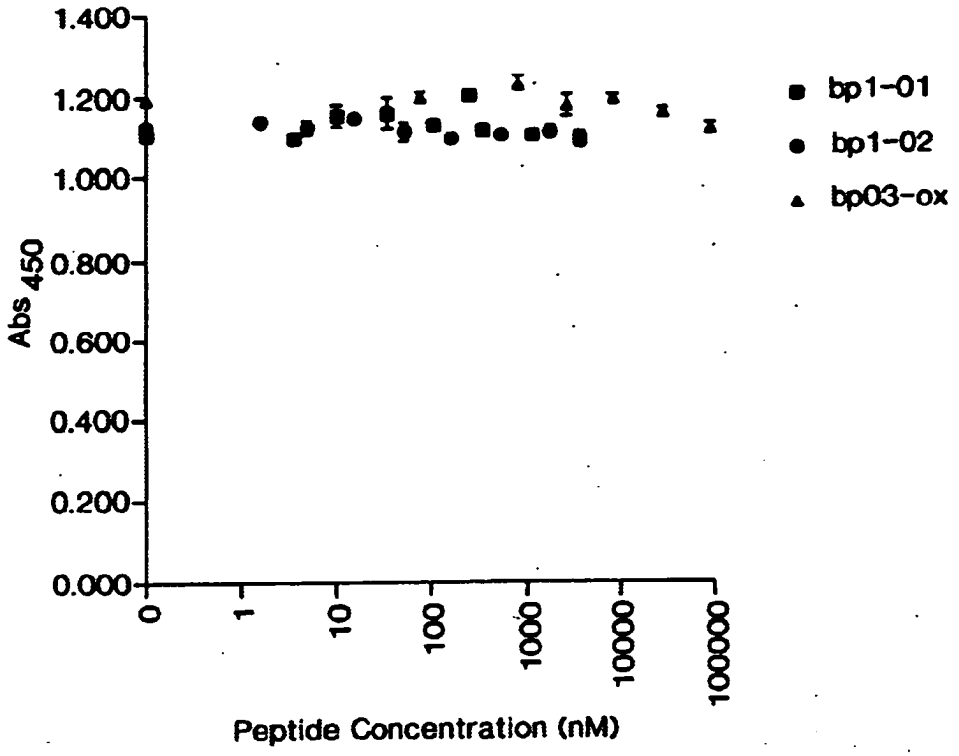

FIG. 37C

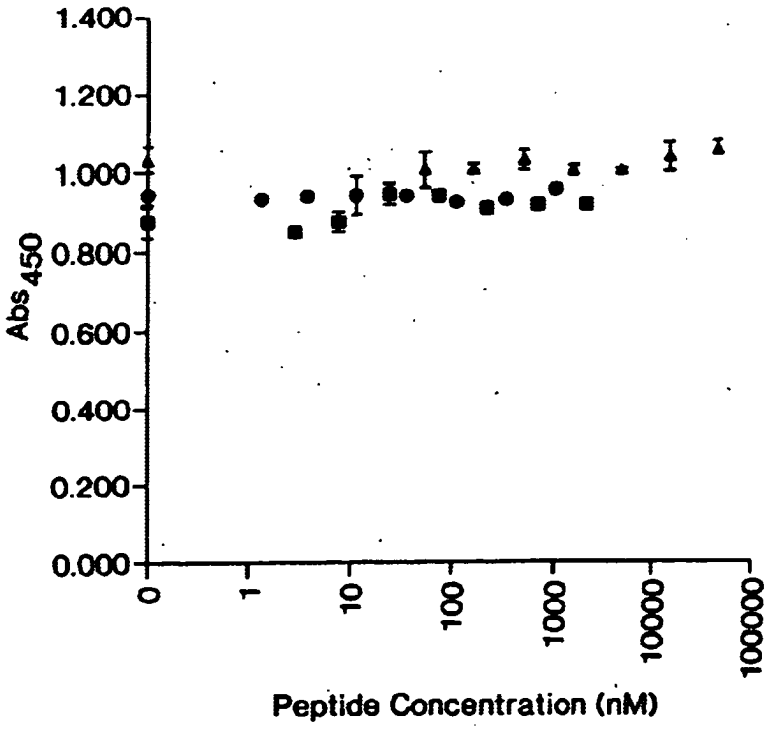

FIG. 37D

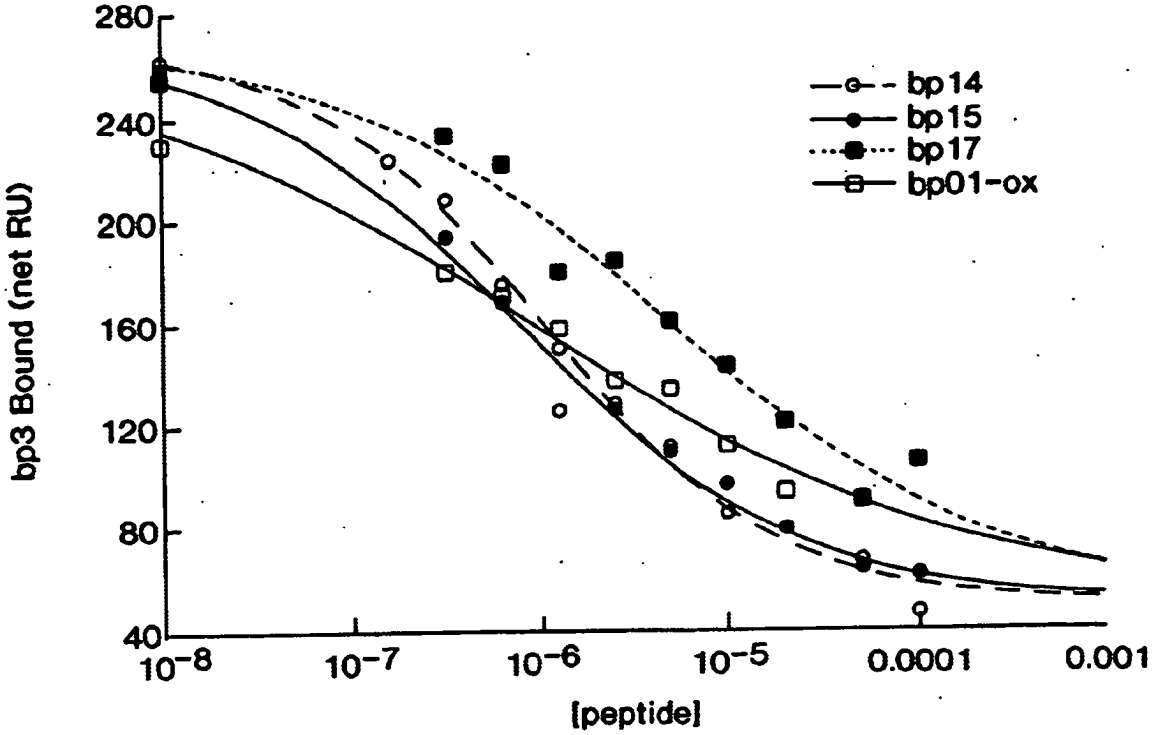

FIG. 38

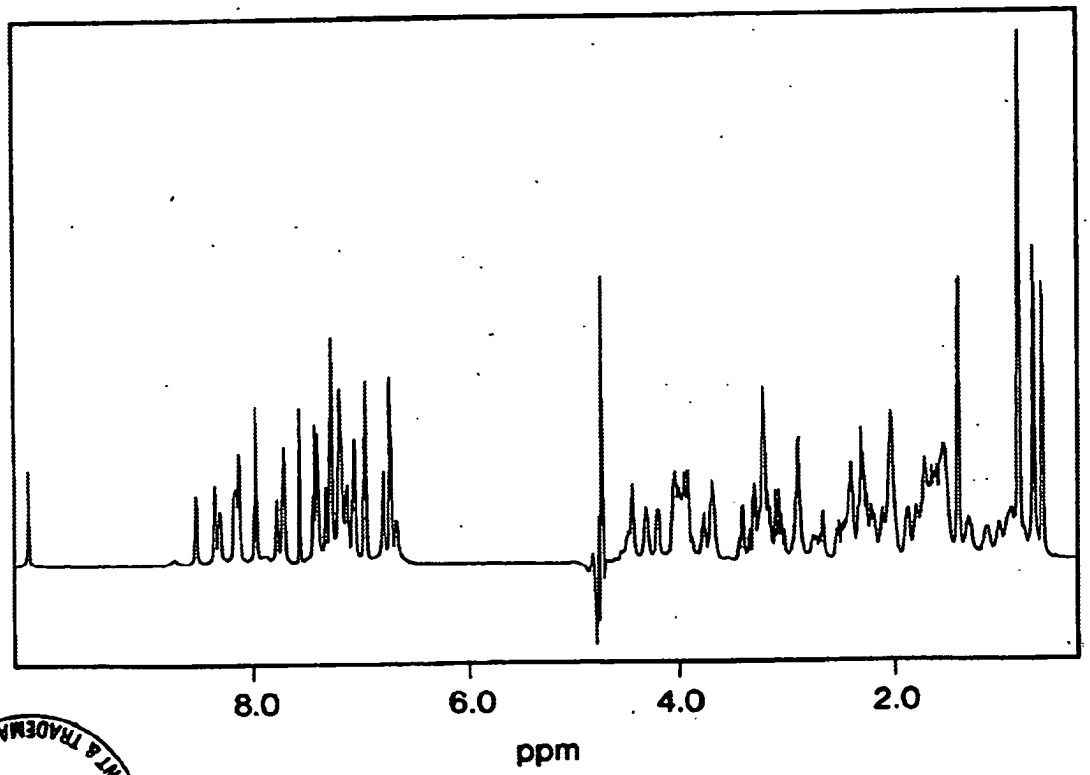

FIG. 39

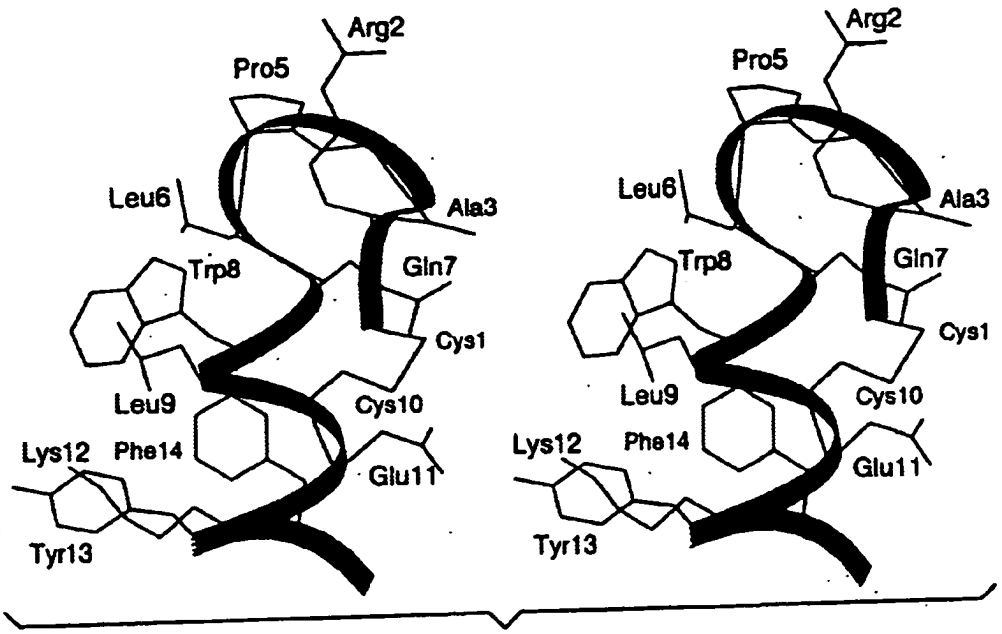

FIG. 40A

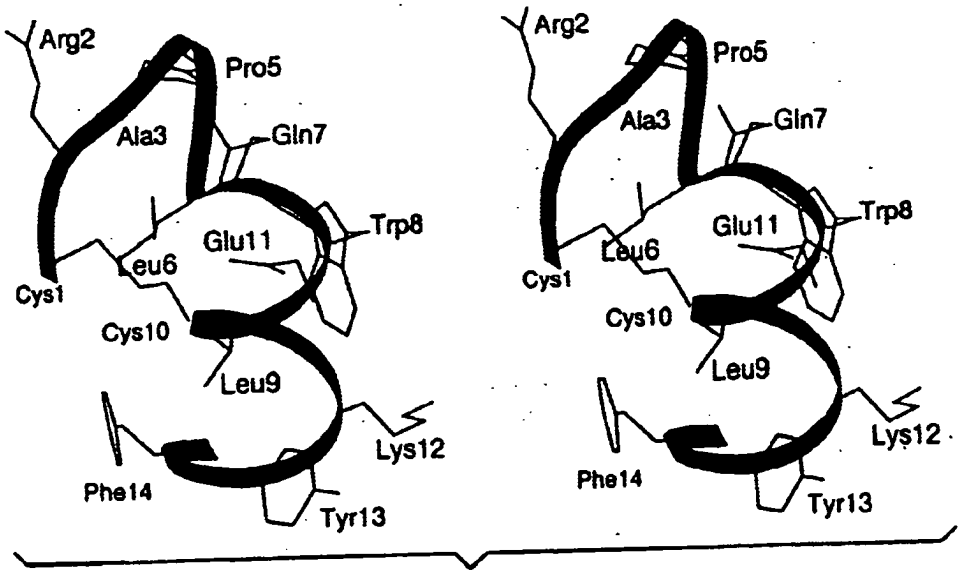

FIG. 40B

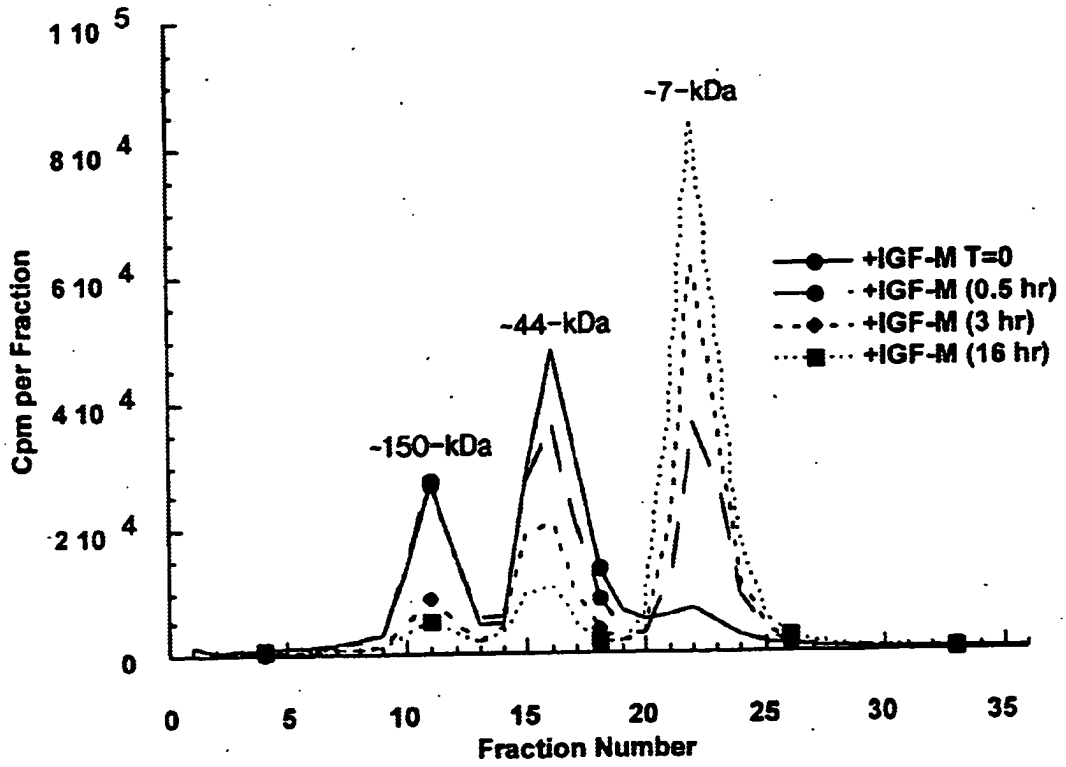

FIG. 41

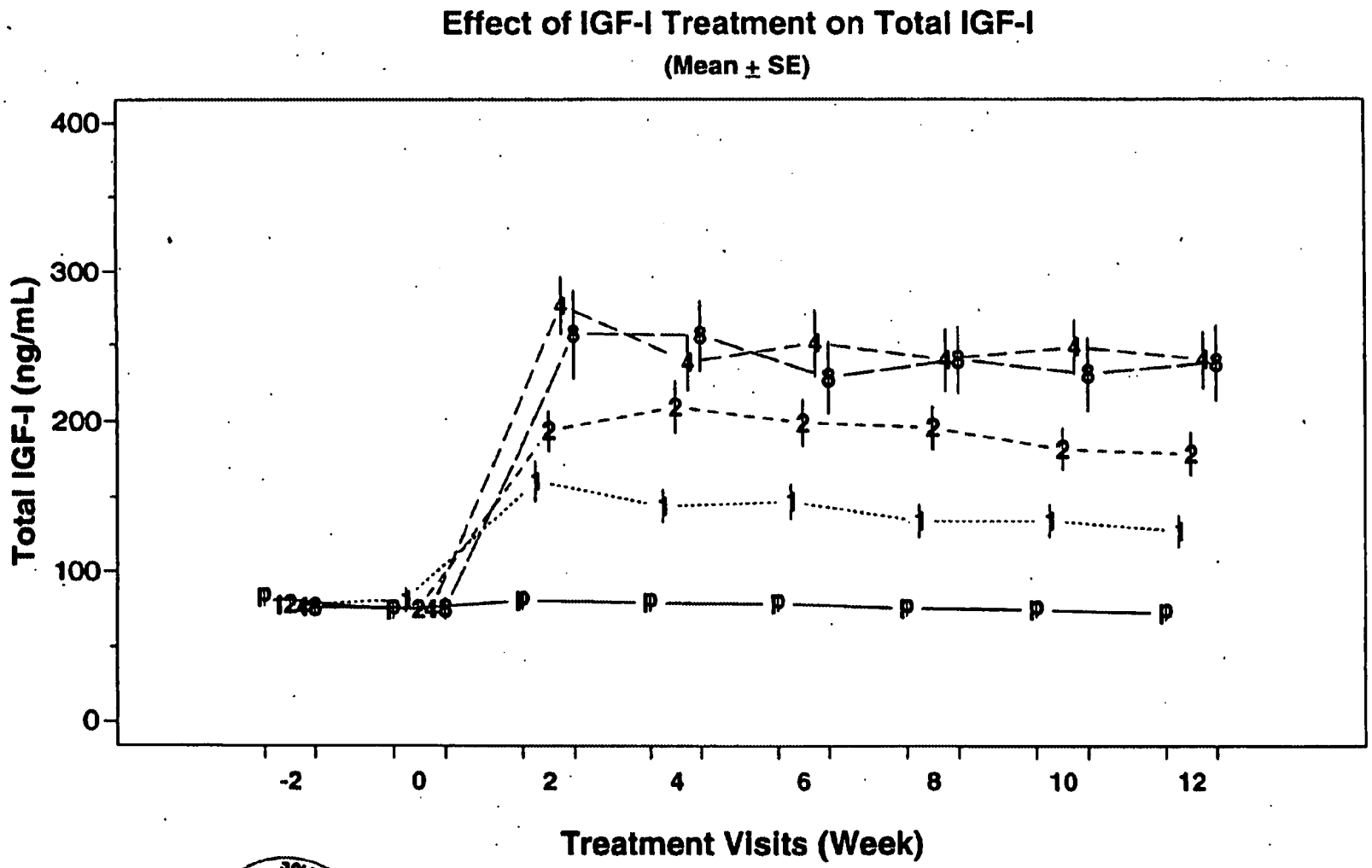

FIG. 42

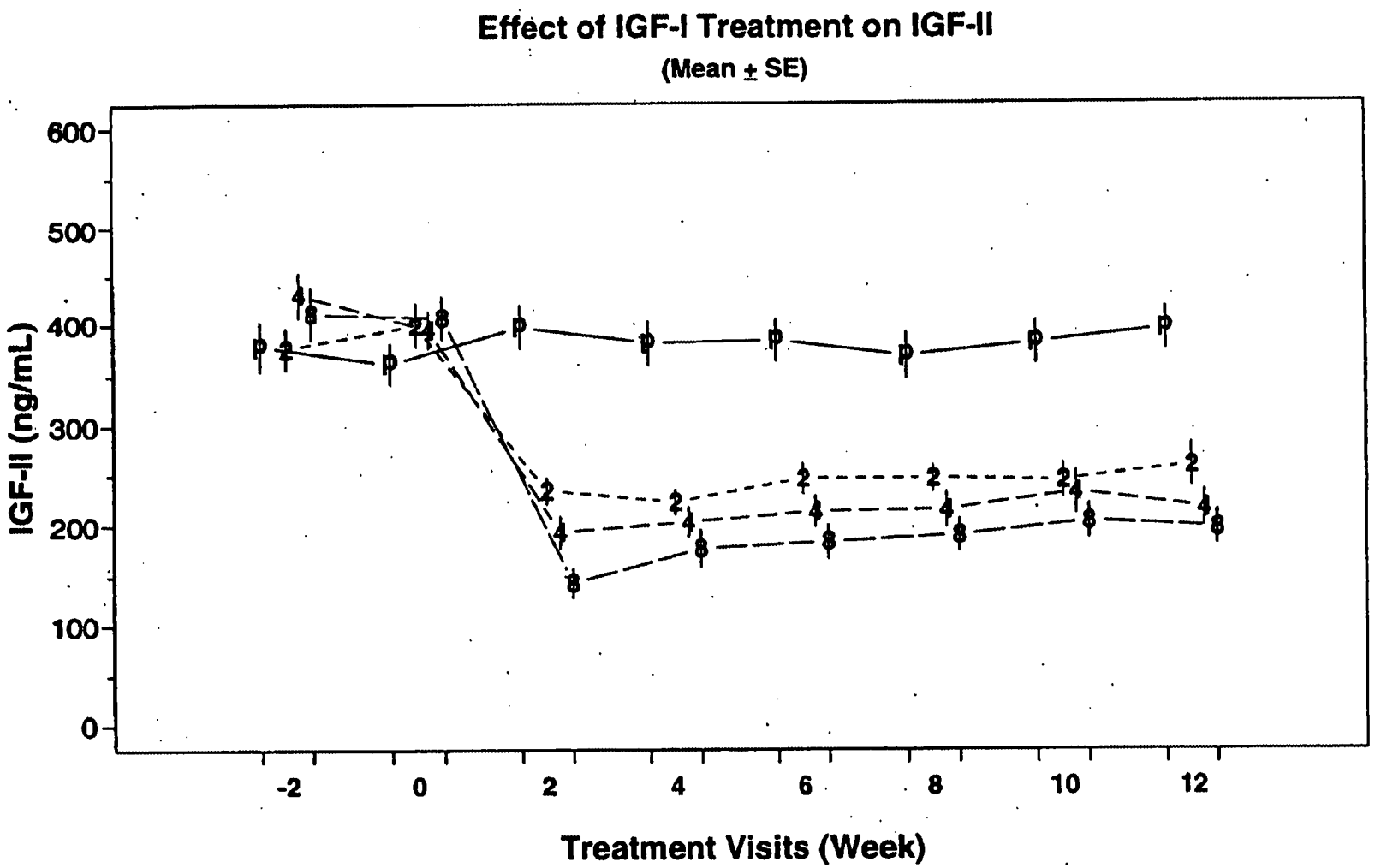

FIG. 43

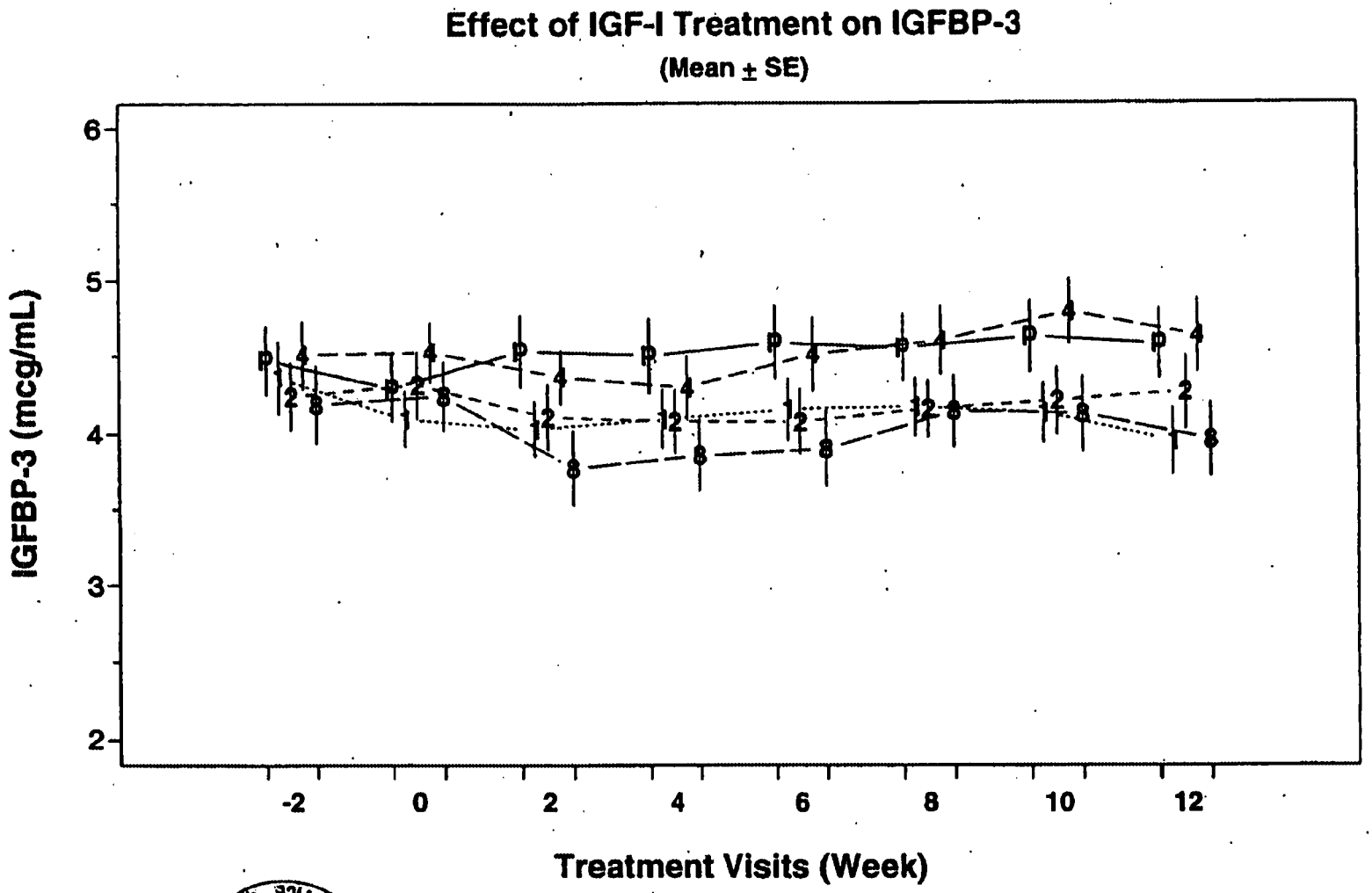

FIG. 44